



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 133999

TO: Rebecca Cook
Location: REM-3C70
Art Unit: 1614
Monday, October 04, 2004

Case Serial Number: 10/694448

From: Mary Jane Ruhl
Location: Biotech-Chem Library
Remsen 1-A-62
Phone: 571-272-2524

maryjane.ruhl@uspto.gov

Search Notes

Examiner Cook,

Here are the results for your recent search request.

Please feel free to contact me if you have any questions about these results.

Thank you for using STIC services. We appreciate the opportunity to serve you.

Sincerely,

Mary Jane Ruhl
Technical Information Specialist
STIC
Remsen 1-A-62
Ext. 22524

=> d his ful

FILE 'REGISTRY' ENTERED AT 11:17:16 ON 04 OCT 2004

E L-METHIONINE/CN

L1 1 SEA ABB=ON L-METHIONINE/CN

E D-METHIONINE/CN

L2 1 SEA ABB=ON D-METHIONINE/CN

E METHIONINE/CN

E S-ADENOSYL-L-METHIONINE/CN

L3 1 SEA ABB=ON S-ADENOSYL-L-METHIONINE/CN

FILE 'HCAPLUS' ENTERED AT 11:17:58 ON 04 OCT 2004

L4 93275 SEA ABB=ON L1 OR L2 OR L3 OR ?METHIONINE? OR S(W)?ADENOSYL?(W)
L(W)?METHIONINE?

FILE 'REGISTRY' ENTERED AT 11:18:33 ON 04 OCT 2004

E PLATINUM

E PLATINUM/CN

L5 1 SEA ABB=ON PLATINUM/CN

FILE 'HCAPLUS' ENTERED AT 11:18:46 ON 04 OCT 2004

L6 511 SEA ABB=ON L4 AND (L5 OR PT OR ?PLATINUM?)

L7 18 SEA ABB=ON L6 AND (?CHEMOTHER? OR ?ANTI?(W) (?TUMOR? OR
?TUMOUR?))

D AU 1-18

SELECT RN L7 1-18

FILE 'REGISTRY' ENTERED AT 11:28:38 ON 04 OCT 2004

ACT COO432L22/L

L8 STR

FILE 'HCAPLUS' ENTERED AT 11:29:09 ON 04 OCT 2004

SET SMARTSELECT ON

L9 SEL L7 1- RN : 201 TERMS

SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 11:29:10 ON 04 OCT 2004

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L11 0 SEA SUB=L10 SSS SAM L8

L12 0 SEA SUB=L10 SSS FUL L8

FILE 'HCAPLUS' ENTERED AT 11:31:19 ON 04 OCT 2004

SELECT RN L7 1-18

FILE 'REGISTRY' ENTERED AT 11:32:35 ON 04 OCT 2004

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 2897-21-4/BI OR 2922-56

FILE 'HCAPLUS' ENTERED AT 11:33:10 ON 04 OCT 2004

L14 18 SEA ABB=ON L7 AND L13
 L15 6 SEA ABB=ON L14 AND (?OTOTOX? OR EAR? OR ?HEAR? OR ?OTOLOG? OR
 ?OTOLARYNG?)
 L16 18 SEA ABB=ON L14 OR L15
 L17 15 SEA ABB=ON L16 AND (?PATIENT? OR ?HUMAN? OR MAN? OR CAT? OR
 ?FELINE? OR DOG? OR ?CANINE?)
 L18 18 SEA ABB=ON L16 OR L17
 L19 18 SEA ABB=ON L18 AND (?PREVENT? OR ?TREAT? OR ?INHIBIT? OR
 ?SUPPRES? OR ?RESIST? OR ?THERAP? OR ?CONTROL? OR ?HEAL? OR
 ?MEDICIN? OR ?PHARM?)
 L20 8 SEA ABB=ON L19 AND (?METHOD? OR ?TECHNIQ?)
 L21 18 SEA ABB=ON L19 OR L20
 SET SMARTSELECT ON
 L22 SEL L6 1- RN : 7935 TERMS
 SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 11:39:55 ON 04 OCT 2004

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 L24 0 SEA SUB=L23 SSS SAM L8
 L25 2 SEA SUB=L23 SSS FUL L8

FILE 'HCAPLUS' ENTERED AT 11:41:12 ON 04 OCT 2004

L26 421 SEA ABB=ON L25
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 ?MEDICIN? OR ?PHARM?)
 L30 3 SEA ABB=ON L27 AND (?METHOD? OR ?TECHNIQ?)
 L31 20 SEA ABB=ON L27 OR L28 OR L29 OR L30
 L32 38 SEA ABB=ON L21 OR L31
 L33 26 SEA ABB=ON L32 AND (?OTOTOX? OR EAR? OR ?HEAR? OR ?OTOLOG? OR
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*26 cit's from CAPLUS, from
 structure/test search + test search*

=> d que stat 133

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L1      1 SEA FILE=REGISTRY ABB=ON  L-METHIONINE/CN
L2      1 SEA FILE=REGISTRY ABB=ON  D-METHIONINE/CN
L3      1 SEA FILE=REGISTRY ABB=ON  S-ADENOSYL-L-METHIONINE/CN
L4      93275 SEA FILE=HCAPLUS ABB=ON  L1 OR L2 OR L3 OR ?METHIONINE? OR
        S(W)?ADENOSYL?(W)L(W)?METHIONINE?
L5      1 SEA FILE=REGISTRY ABB=ON  PLATINUM/CN
L6      511 SEA FILE=HCAPLUS ABB=ON  L4 AND (L5 OR PT OR ?PLATINUM?)
L7      18 SEA FILE=HCAPLUS ABB=ON  L6 AND (?CHEMOTHER? OR ?ANTI?(W)(?TUMO
        R? OR ?TUMOUR?))
L8      STR

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      7
      G3      Ak~N~Ak
      }      8 @9 10
H3C~G1~S~G2~CH~G4
  1  2  3  4  5  6

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REP G1=(0-3) CH2

REP G2=(1-3) CH2

VAR G3=O/C

VAR G4=9/OH

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M1-X6 C AT 8

ECOUNT IS M1-X6 C AT 10

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

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 169277-44-5/BI OR 171715-28-9/BI OR 177258-45-6/BI OR 1951-25-3
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 L14 18 SEA FILE=HCAPLUS ABB=ON L7 AND L13
 L15 6 SEA FILE=HCAPLUS ABB=ON L14 AND (?OTOTOX? OR EAR? OR ?HEAR?
 OR ?OTOLOG? OR ?OTOLARYNG?)
 L16 18 SEA FILE=HCAPLUS ABB=ON L14 OR L15
 L17 15 SEA FILE=HCAPLUS ABB=ON L16 AND (?PATIENT? OR ?HUMAN? OR MAN?
 OR CAT? OR ?FELINE? OR DOG? OR ?CANINE?)
 L18 18 SEA FILE=HCAPLUS ABB=ON L16 OR L17
 L19 18 SEA FILE=HCAPLUS ABB=ON L18 AND (?PREVENT? OR ?TREAT? OR
 ?INHIBIT? OR ?SUPPRES? OR ?RESIST? OR ?THERAP? OR ?CONTROL? OR
 ?HEAL? OR ?MEDICIN? OR ?PHARM?)
 L20 8 SEA FILE=HCAPLUS ABB=ON L19 AND (?METHOD? OR ?TECHNIQ?)
 L21 18 SEA FILE=HCAPLUS ABB=ON L19 OR L20
 L22 SEL L6 1- RN : 7935 TERMS
 L23 7935 SEA FILE=REGISTRY ABB=ON L22
 L25 2 SEA FILE=REGISTRY SUB=L23 SSS FUL L8
 L26 421 SEA FILE=HCAPLUS ABB=ON L25
 L27 20 SEA FILE=HCAPLUS ABB=ON L26 AND (?OTOTOX? OR EAR? OR ?HEAR?
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 L28 13 SEA FILE=HCAPLUS ABB=ON L27 AND (?PATIENT? OR ?HUMAN? OR MAN?
 OR CAT? OR ?FELINE? OR DOG? OR ?CANINE?)
 L29 10 SEA FILE=HCAPLUS ABB=ON L27 AND (?PREVENT? OR ?TREAT? OR
 ?INHIBIT? OR ?SUPPRES? OR ?RESIST? OR ?THERAP? OR ?CONTROL? OR
 ?HEAL? OR ?MEDICIN? OR ?PHARM?)
 L30 3 SEA FILE=HCAPLUS ABB=ON L27 AND (?METHOD? OR ?TECHNIQ?)
 L31 20 SEA FILE=HCAPLUS ABB=ON L27 OR L28 OR L29 OR L30
 L32 38 SEA FILE=HCAPLUS ABB=ON L21 OR L31
 L33 26 SEA FILE=HCAPLUS ABB=ON L32 AND (?OTOTOX? OR EAR? OR ?HEAR?
 OR ?OTOLOG? OR ?OTOLARYNG?)

=> d ibib abs hitstr 133 1-26

L33 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:298909 HCAPLUS

DOCUMENT NUMBER: 141:70850

TITLE: Feeding 2-hydroxy-4-(methylthio)-butanoic acid to periparturient dairy cows improves milk production but not hepatic metabolism

AUTHOR(S): Piepenbrink, M. S.; Marr, A. L.; Waldron, M. R.; Butler, W. R.; Overton, T. R.; Vazquez-Anon, M.; Holt, M. D.

CORPORATE SOURCE: Department of Animal Science, Cornell University, Ithaca, NY, 14853, USA

SOURCE: Journal of Dairy Science (2004), 87(4), 1071-1084
CODEN: JDSCAE; ISSN: 0022-0302

PUBLISHER: American Dairy Science Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Holstein dairy cows (n=48) entering second or later lactation were used to determine the effects of 2-hydroxy-4-(methylthio)butanoic acid (HMB, methionine hydroxy analog) on milk production, hepatic lipid metabolism, and gluconeogenesis

during the periparturient period. The cows were fed 3 diets as total mixed rations starting 21 days before expected calving. The diets contained 0 (basal diet), 0.09 (+HMB), or 0.18 (++)HMB% HMB. From parturition to 84 days in milk, the cows were fed diets with 0, 0.13, or 0.20% HMB. Prepartum and postpartum dry matter intakes were similar among cows fed the basal, +HMB, and ++HMB diets. There was a quadratic effect on milk yield such that cows fed +HMB had the greatest milk yield; yields of milk in cows fed the basal and ++HMB diets were similar. This led to trends for increased yields of 3.5% fat-corrected milk and total milk solids when cows were fed +HMB diet. The % of milk fat, protein, and total solids were not affected by dietary treatments. Despite differences in milk yield, the calculated energy balance was not affected by dietary treatments. Blood plasma concns. of nonesterified fatty acids, β -hydroxybutyrate, and glucose were not different among the treatments. Liver triglyceride contents were similar among treatments on day 1 postpartum and were increased in cows fed +HMB diet on day 21 postpartum compared to the other dietary treatments. The capacities for metabolism of [1-14C]palmitate by liver slices in vitro were not affected by treatments, but the conversion of [1-14C]propionate to CO₂ and glucose decreased as the amount of HMB fed increased on day 21 postpartum. Cows fed +HMB had greater days-to-first ovulation compared with cows fed the basal and ++HMB diets as measured by blood plasma progesterone concns. Thus, adding HMB to low-methionine diets to achieve methionine level of .apprx.2.3% of metabolizable protein supply is beneficial for increasing milk production, but does not appear to benefit hepatic energy metabolism during early lactation.

IT 583-91-5, 2-Hydroxy-4-(methylthio)-butanoic acid

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)

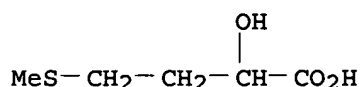
(dietary 2-hydroxy-4-(methylthio)butanoic acid (methionine hydroxy analog) improves milk production but not hepatic metabolism in

periparturient

(Holstein dairy cows)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2004:220127 HCAPLUS
 DOCUMENT NUMBER: 140:270109
 TITLE: Use of metal chelates in **human** or animal feeding
 INVENTOR(S): Cinti, Enrico; Ciribolla, Antonio
 PATENT ASSIGNEE(S): Agristudio S.R.L., Italy
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004021802	A2	20040318	WO 2003-IT400	20030627
WO 2004021802	A3	20040415		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: IT 2002-RE67 A 20020906
 IT 2003-MI863 A 20030429

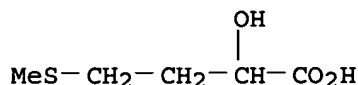
AB The present invention relates to the use in **human** and animal nutrition (monogastric and polygastric animals) of known chelates of bivalent metal Mg, Ca, Mn, Co, Cu, Zn and Fe with methionine hydroxy analog. The present invention further relates to a **method** for preparing new chelates with methionine hydroxy analog, both in solid form with iron (II), vanadium (IV) and (V) and molybdenum (V) and (VI), and in liquid form in aqueous solution with iron (II) and (III) and chrome (III). Eventually, the present invention relates to the use of said new chelates, both in solid form with iron (II), vanadium (IV) and (V) and molybdenum (V) and (VI), and in liquid form in aqueous solution with iron (II) and (III)

and chrome (III), in **human** and animal nutrition.

IT 583-91-5DP, metal complexes
 RL: FFD (Food or feed use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (use of metal chelates in **human** or animal feeding)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:912094 HCAPLUS

DOCUMENT NUMBER: 140:145274

TITLE: Adaptations in body muscle and fat in transition dairy cattle fed differing amounts of protein and methionine hydroxy analog

AUTHOR(S): Phillips, G. J.; Citron, T. L.; Sage, J. S.; Cummins, K. A.; Cecava, M. J.; McNamara, J. P.

CORPORATE SOURCE: CH2M Hill, Hanford, WA, USA

SOURCE: Journal of Dairy Science (2003), 86(11), 3634-3647

CODEN: JDSCAE; ISSN: 0022-0302

PUBLISHER: American Dairy Science Association

DOCUMENT TYPE: Journal

LANGUAGE: English

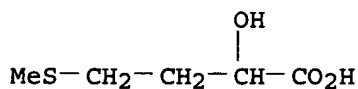
AB The effects of prepartum dietary protein intake and dietary amino acid balance on milk production, adaptations in body fat, and blood serum protein and amino acid concns. (and indirectly body protein breakdown) in early lactation were studied in 42 multiparous Holstein dairy cows. The cows were fed diets containing 11 or 14% crude protein (CP) with or without 20 g methionine hydroxy analog daily for 21 days prepartum and then were fed common diet with 17% CP for 120 days postpartum, with or without 50 g methionine hydroxy analog (Rhodimet AT-88) daily. The dry matter (DM) intake postpartum averaged 25.4 kg and milk production 41.6 kg. Cows fed the 14% CP diet ate 0.7 kg more DM and gave 1.7 kg more milk than those fed the 11% CP diet prepartum. Cows fed the methionine hydroxy analog prepartum lost less body protein from -14 to +60 days in milk. From day 60 to 120, body fat increased 8.5 and 11.5 kg in low- and high-protein groups and body protein increased 0.5 and 1.0 kg. Blood serum concns. of branched-chain amino acids fell 17% in the first few weeks postpartum, lysine fell 15%, histidine fell 16%, methionine increased 20%, and cysteine increased 30%. The serum 3-methylhistidine/creatinine ratio was determined to indicate muscle protein degradation. An increase in this ratio 7 days postpartum indicated increased body protein breakdown and there was no effect of prepartum ration composition. Increased protein intake prepartum may allow more feed intake and milk production postpartum. Supplementing the methionine analog to a ration already balanced in methionine by contemporary models may spare body protein.

IT 583-91-5

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
 (diets with differing amts. of protein and methionine hydroxy analog effects on adaptations in body muscle and fat in transition Holstein dairy cows)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:590714 HCAPLUS
 DOCUMENT NUMBER: 139:148557
 TITLE: Protease **catalyzed** enantioselective
 oligomerization of α -hydroxy carboxylic acids
 and α -amino acids
 INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul
 K.S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila,
 Shubhender
 PATENT ASSIGNEE(S): Novus International, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S.
 Ser. No. 699,946.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003143661	A1	20030731	US 2002-136974	20020502
US 6605590	B1	20030812	US 2000-699946	20001030
US 2004048347	A1	20040311	US 2003-609825	20030630
PRIORITY APPLN. INFO.:			US 1999-162725P	P 19991029
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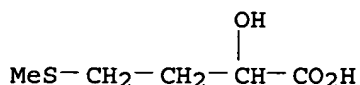
OTHER SOURCE(S): MARPAT 139:148557

AB An enzymic synthesis and composition of oligomers and co-oligomers comprised of α -hydroxy carboxylic acids and α -amino acids or peptides is disclosed. In a preferred embodiment, a α -hydroxy carboxylic acid with a specific chiral configuration is linked by an amide linkage to a α -amino acid specific with a specific chiral configuration or linked by an amide linkage to a peptide made up of α -amino acid monomers having identical chiral configurations. Proteolytic enzymes **catalyze** oligomerization of the α -hydroxy carboxylic acid and α -amino acid. The degree and distribution of oligomerization varies upon the type and concns. of different reaction mixts. utilized and upon the length of allowed reaction time. The resultant oligomers may be provided to animals such as ruminants as bioavailable amino acid supplements that are **resistant** to degradation in the rumen and other animals such as swine, poultry and aquatic animals.

IT **583-91-5D**, 2-Hydroxy-4-(methylthio)butyric acid, and derivs. of
 RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);
 PROC (Process); RACT (Reactant or reagent)
 (protease **catalyzed** enantioselective oligomerization of
 α -hydroxy carboxylic acids and α -amino acids)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:428146 HCAPLUS
 DOCUMENT NUMBER: 139:322807

TITLE: Effect of feeding methionine supplements with different rumen escape values on performance of high producing dairy cows in **early** lactation

AUTHOR(S): Uchida, K.; Mandevu, P.; Ballard, C. S.; Sniffen, C. J.; Carter, M. P.

CORPORATE SOURCE: W.H. Miner Agricultural Research Institute, Chazy, NY, 12921-0090, USA

SOURCE: Animal Feed Science and Technology (2003), 107(1-4), 1-14
CODEN: AFSTDH; ISSN: 0377-8401

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

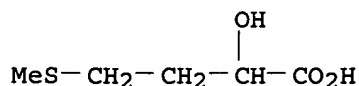
LANGUAGE: English

AB A study was undertaken to compare a liquid form of methionine hydroxy analog (MHA; Novus Intl., Atlanta, GA, USA) and d,l-methionine, two methionine supplements with different rumen degradation escape values, on **early** lactational and reproductive performance by high producing dairy cows. Forty pregnant Holstein cows housed in a free-stall barn, were blocked by parity, date of calving, and previous 305-day mature equivalent milk production, and at calving were assigned randomly to one of two total mixed rations (TMR) containing MHA, or d,l-methionine, and group-fed for ad libitum intake. Cows spent 33±15.0 days in the fresh group, after which they were moved to the high producing group where they stayed up to 8-wk postpartum. The TMR were formulated to meet approx. 100% of required methionine, lysine, and other essential amino acids. An adequate amount of d,l-methionine was fed in order to provide a similar amount of methionine postruminally as provided by MHA, assuming a rumen degradation escape value of 40% for MHA and 22% for d,l-methionine. The TMR had forage to concentrate ratio of 40 to 60% for fresh group cows and 42 to 58% for high group cows. There were no differences between **treatments** in milk yield, content of milk fat, CP and true protein, linear somatic cell count, change in body condition score, and days to first service. In conclusion, d,l-methionine performed as well as MHA in promoting milk yield and contents of milk fat and protein when fed at levels aimed at supplying similar amts. of methionine postruminally as would be supplied by MHA fed at the recommended level.

IT 583-91-5
RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of feeding Met supplements with different rumen escape values on performance of high producing dairy cows in **early** lactation)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:537491 HCAPLUS

DOCUMENT NUMBER: 135:117260

TITLE: **Therapeutic use of D-methionine to reduce the toxicity of ototoxic drugs, noise, and radiation**

INVENTOR(S): Campbell, Kathleen C. M.
 PATENT ASSIGNEE(S): Southern Illinois University School of Medicine, USA
 SOURCE: U.S., 23 pp., Cont.-in-part of U.S. 6,187,817.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6265386	B1	20010724	US 1998-57065	19980408
US 6187817	B1	20010213	US 1997-942845	19971002
PT 1019036	T	20031128	PT 1998-915362	19980408
ES 2202834	T3	20040401	ES 1998-915362	19980408
US 2002019443	A1	20020214	US 2001-911195	20010723
US 2004110719	A1	20040610	US 2003-694448	20031027
US 2004127568	A1	20040701	US 2003-694432	20031027
PRIORITY APPLN. INFO.:			US 1997-942845	A2 19971002
			US 1996-27750P	P 19961003
			US 1998-57065	A2 19980408
			US 2001-911195	A1 20010723

AB **Methods of preventing or reducing hearing or balance loss, damage to ear cells, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and prolonging survival in patients undergoing treatment with therapeutically effective amts. of platinum-containing chemotherapeutic agents such as cisplatin are provided. Methods are also provided for preventing or reducing such symptoms in patients undergoing treatment with loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, and quinidine, or those who have been exposed to toxic levels of noise or radiation. These methods comprise administering an effective amount of a methionine protective agent, such as D-methionine, prior to, simultaneously with, or subsequently to administration of the platinum-containing chemotherapeutic agent, loop diuretic agent, etc., or exposure to noise or radiation. Combinations of these time periods can also be employed.**

IT 7439-89-6, Iron, biological studies
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (chelating agents; therapeutic use of D-methionine and related compds. to reduce toxicity of ototoxic drugs, noise, platinum-containing antitumor drugs, and radiation)

RN 7439-89-6 HCAPLUS
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT 56-54-2, Quinidine 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 114-07-8, Erythromycin 130-95-0, Quinine 1403-66-3, Gentamicin 1404-04-2, Neomycin 1404-90-6, Vancomycin 6379-56-2, Hygromycin 7542-37-2, Paromomycin 14096-51-6, Dichloro(ethylenediamine)platinum(II) 14215-58-8, Chloro(diethylenetriamine)platinum(II) chloride 14913-33-8, trans-Diamminedichloroplatinum (II) 15663-27-1, Cisplatin 20115-64-4

32986-56-4, Tobramycin 37517-28-5, Amikacin
 41575-93-3 41575-94-4, Carboplatin 41666-77-7
 56391-56-1, Netilmicin 62928-11-4, Iproplatin
 64363-09-3 67254-31-3 74790-08-2, Spiroplatin
 114579-59-8 141610-50-6 148977-78-0
 149055-58-3

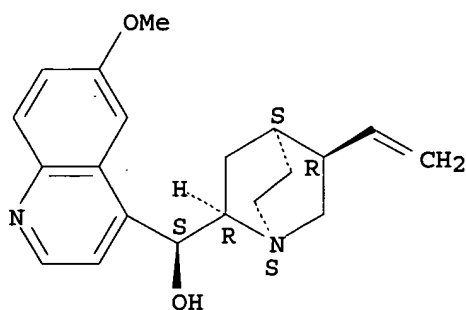
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(therapeutic use of D-methionine and related
 compds. to reduce toxicity of ototoxic drugs, noise,
 platinum-containing antitumor drugs, and radiation)

RN 56-54-2 HCAPLUS

CN Cinchonan-9-ol, 6'-methoxy-, (9S)- (9CI) (CA INDEX NAME)

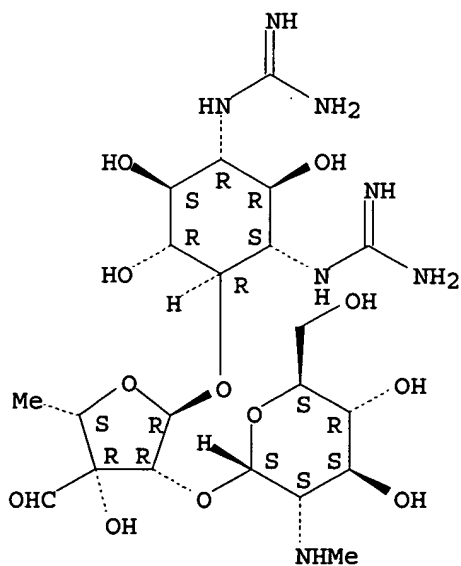
Absolute stereochemistry. Rotation (+).



RN 57-92-1 HCAPLUS

CN D-Streptamine, O-2-deoxy-2-(methylamino)- α -L-glucopyranosyl-
 (1 \rightarrow 2)-O-5-deoxy-3-C-formyl- α -L-lyxofuranosyl-(1 \rightarrow 4)-
 N,N'-bis(aminoiminomethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

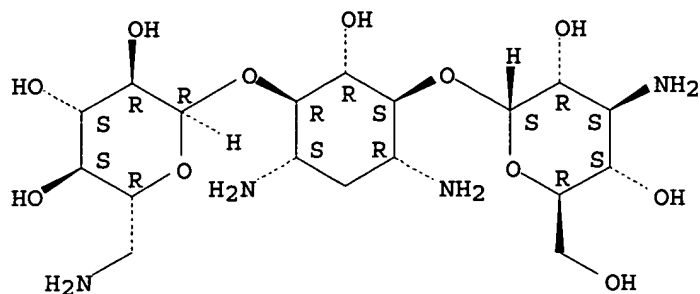


RN 59-01-8 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-

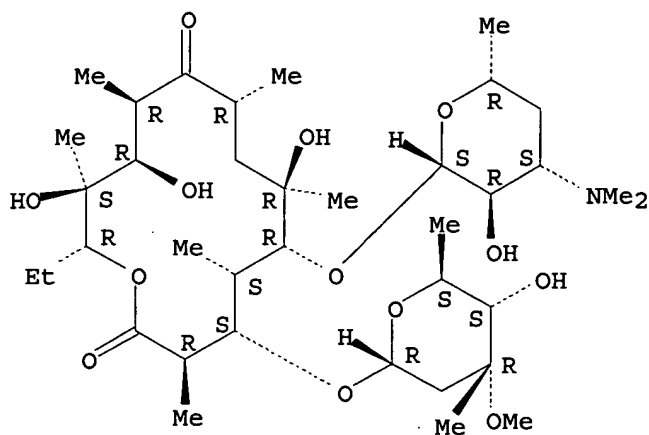
[6-amino-6-deoxy- α -D-glucopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



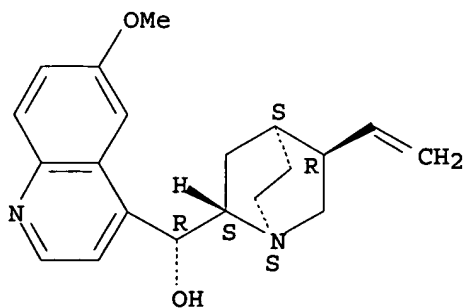
RN 114-07-8 HCAPLUS
CN Erythromycin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 130-95-0 HCAPLUS
CN Cinchonan-9-ol, 6'-methoxy-, (8 α ,9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 1403-66-3 HCAPLUS
CN Gentamicin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 1404-04-2 HCAPLUS

CN Neomycin (9CI) (CA INDEX NAME)

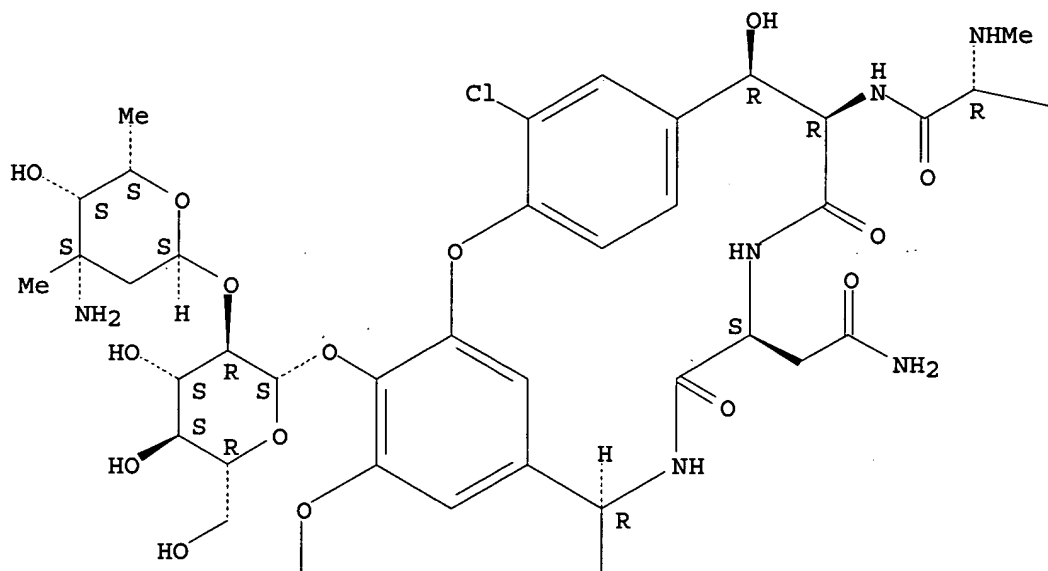
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 1404-90-6 HCAPLUS

CN Vancomycin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

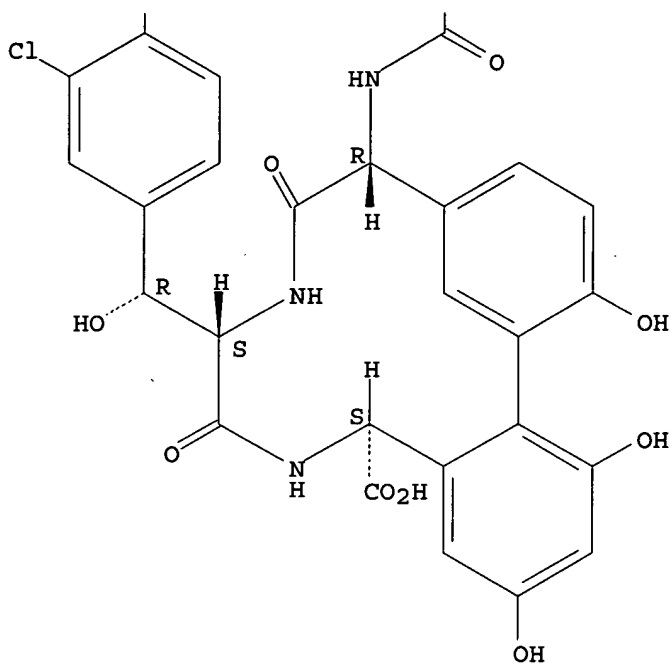
PAGE 1-A



PAGE 1-B

Bu-i

PAGE 2-A

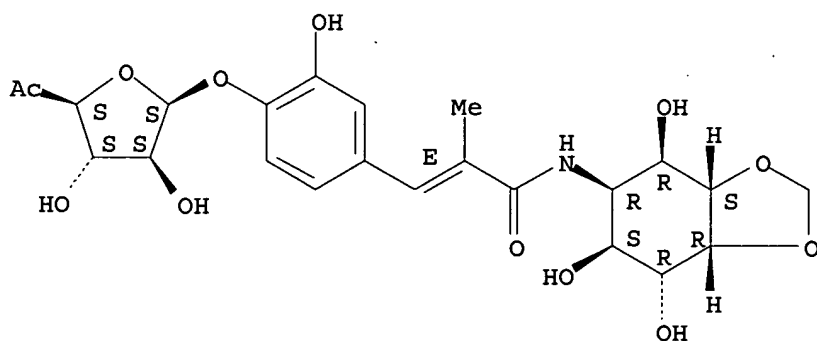


RN 6379-56-2 HCAPLUS

CN D-neo-Inositol, 5-deoxy-5-[[(2E)-3-[4-[(6-deoxy-β-D-arabino-hexofuranos-5-ulos-1-yl)oxy]-3-hydroxyphenyl]-2-methyl-1-oxo-2-propenyl]amino]-1,2-O-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

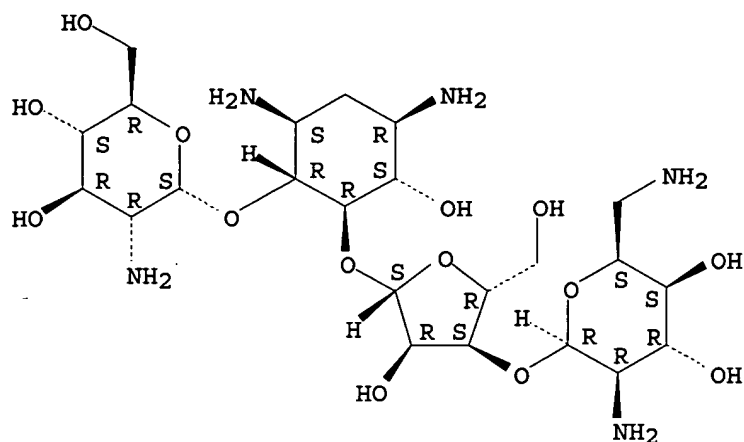
Double bond geometry as shown.



RN 7542-37-2 HCAPLUS

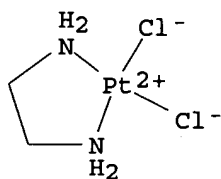
CN D-Streptamine, O-2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)-O-[O-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1→3)-β-D-ribofuranosyl-(1→5)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



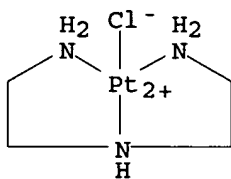
RN 14096-51-6 HCAPLUS

CN Platinum, dichloro(1,2-ethanediamine-κN,κN')-, (SP-4-2)- (9CI)
(CA INDEX NAME)



RN 14215-58-8 HCAPLUS

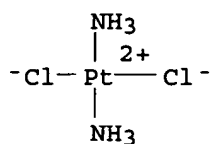
CN Platinum(1+), [N-[2-(amino-κN)ethyl]-1,2-ethanediamine-κN,κN']chloro-, chloride, (SP-4-2)- (9CI) (CA INDEX NAME)



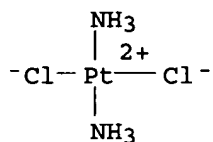
● Cl⁻

RN 14913-33-8 HCAPLUS

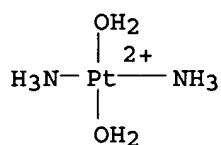
CN Platinum, diamminedichloro-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 15663-27-1 HCAPLUS
 CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)

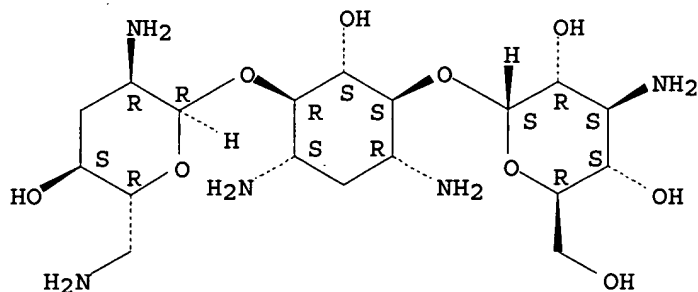


RN 20115-64-4 HCAPLUS
 CN Platinum(2+), diamminediaqua-, (SP-4-2)- (9CI) (CA INDEX NAME)



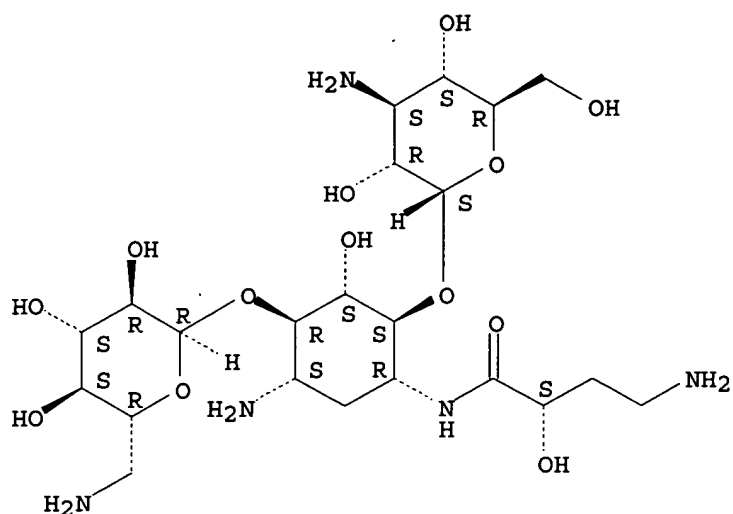
RN 32986-56-4 HCAPLUS
 CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



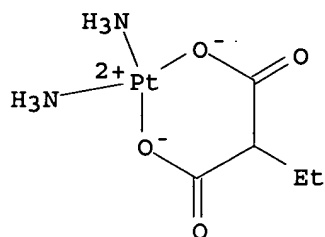
RN 37517-28-5 HCAPLUS
 CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[6-amino-6-deoxy- α -D-glucopyranosyl-(1 \rightarrow 4)]-N1-[(2S)-4-amino-2-hydroxy-1-oxobutyl]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



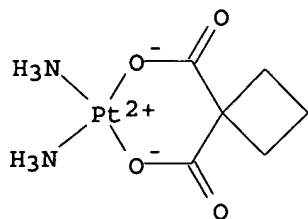
RN 41575-93-3 HCAPLUS

CN Platinum, diammine[ethylpropanedioato(2-)-κO1,κO3]-, (SP-4-2) - (9CI) (CA INDEX NAME)



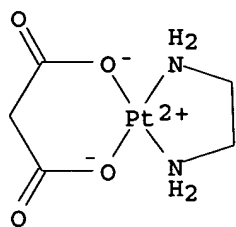
RN 41575-94-4 HCAPLUS

CN Platinum, diammine[1,1-cyclobutanedi(carboxylato-κO)(2-)]-, (SP-4-2) - (9CI) (CA INDEX NAME)



RN 41666-77-7 HCAPLUS

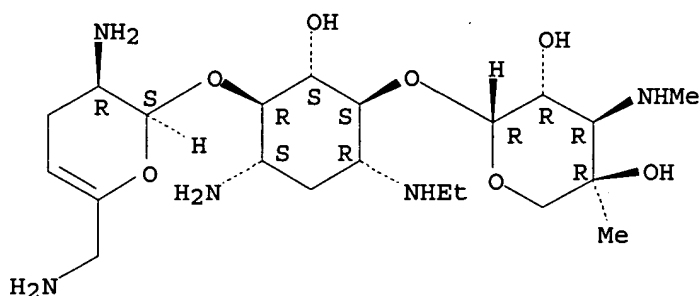
CN Platinum, (1,2-ethanediamine-κN,κN')[propanedioato(2-)-κO1,κO3]-, (SP-4-2) - (9CI) (CA INDEX NAME)



RN 56391-56-1 HCAPLUS

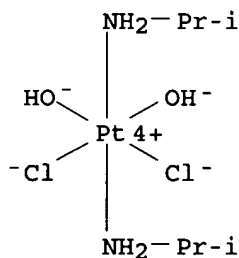
CN D-Streptamine, O-3-deoxy-4-C-methyl-3-(methylamino)- β -L-arabinopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,4,6-tetradeoxy- α -D-glycero-hex-4-enopyranosyl-(1 \rightarrow 4)]-2-deoxy-N1-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



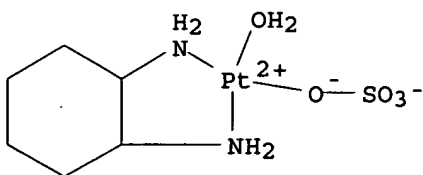
RN 62928-11-4 HCAPLUS

CN Platinum, dichlorodihydroxybis(2-propanamine)-, (OC-6-33)- (9CI) (CA INDEX NAME)

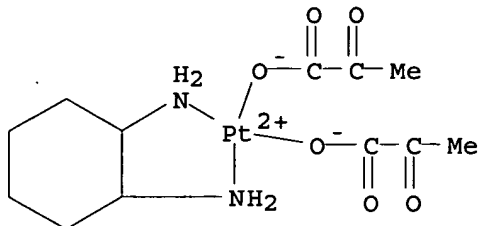


RN 64363-09-3 HCAPLUS

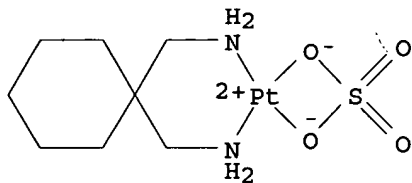
CN Platinum, aqua(1,2-cyclohexanediamine- κ N, κ N') [sulfato(2-)- κ O]-, (SP-4-3)- (9CI) (CA INDEX NAME)



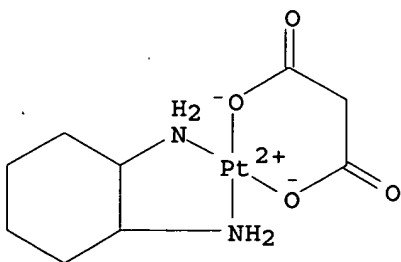
RN 67254-31-3 HCAPLUS
 CN Platinum, (1,2-cyclohexanediamine- κ N, κ N')bis(2-oxopropanoato- κ O)-, (SP-4-2)- (9CI) (CA INDEX NAME)



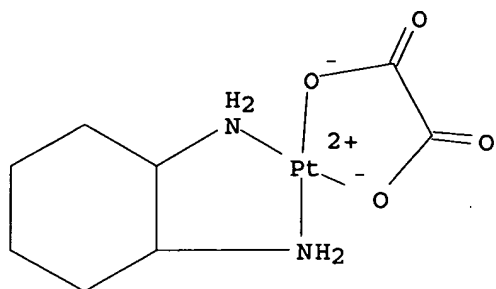
RN 74790-08-2 HCAPLUS
 CN Platinum, (1,1-cyclohexanedimethanamine- κ N, κ N') [sulfato(2-)- κ O, κ O']-, (SP-4-2)- (9CI) (CA INDEX NAME)



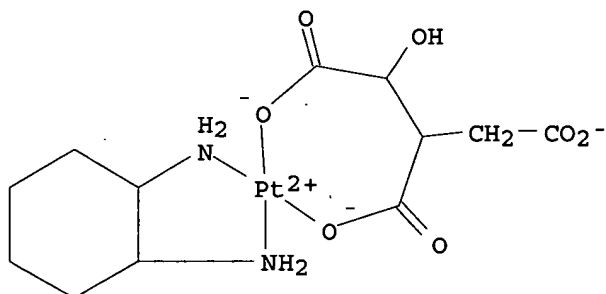
RN 114579-59-8 HCAPLUS
 CN Platinum, (1,2-cyclohexanediamine- κ N, κ N') [propanedioato(2-)- κ O1, κ O3]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 141610-50-6 HCAPLUS
 CN Platinum, (1,2-cyclohexanediamine- κ N, κ N') [ethanedioato(2-)- κ O1, κ O2]-, (SP-4-2)- (9CI) (CA INDEX NAME)

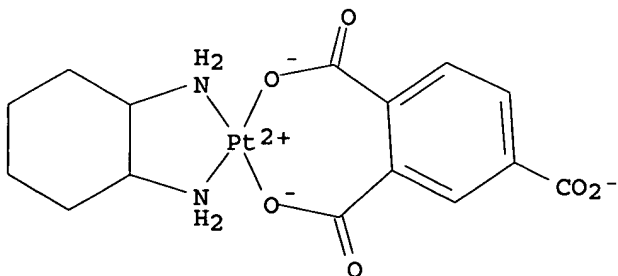


RN 148977-78-0 HCAPLUS
 CN Platinate(1-), (1,2-cyclohexanediamine- κ N, κ N') [1-hydroxy-1,2,3-propanetricarboxylato(3-)- κ O1, κ O2]-, hydrogen, (SP-4-3)- (9CI)
 (CA INDEX NAME)



● H⁺

RN 149055-58-3 HCAPLUS
 CN Platinate(1-), [1,2,4-benzenetricarboxylato(3-)- κ O1, κ O2] (1,2-cyclohexanediamine- κ N, κ N')-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



● H⁺

IT 59-51-8, Methionine 63-68-3, L-
 Methionine, biological studies 348-67-4, D-

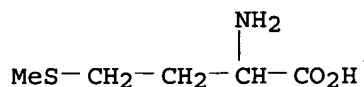
Methionine 502-83-0, Methioninol 1319-79-5
 6094-76-4, Homomethionine 13073-35-3,
 Ethionine 29908-03-0, S-Adenosyl-L
 -methionine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic use of D-methionine and related
 compds. to reduce toxicity of ototoxic drugs, noise,
 platinum-containing antitumor drugs, and radiation)

RN 59-51-8 HCAPLUS

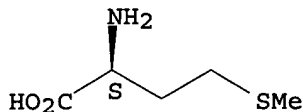
CN Methionine (9CI) (CA INDEX NAME)



RN 63-68-3 HCAPLUS

CN L-Methionine (9CI) (CA INDEX NAME)

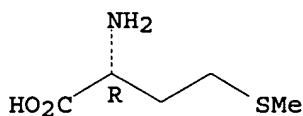
Absolute stereochemistry.



RN 348-67-4 HCAPLUS

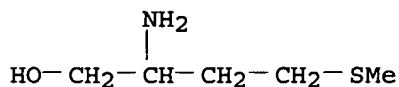
CN D-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



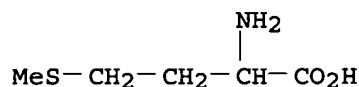
RN 502-83-0 HCAPLUS

CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)



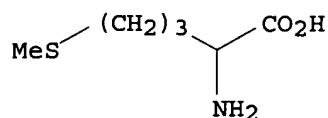
RN 1319-79-5 HCAPLUS

CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)



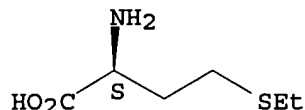
D1-OH

RN 6094-76-4 HCAPLUS
 CN Norvaline, 5-(methylthio)- (9CI) (CA INDEX NAME)



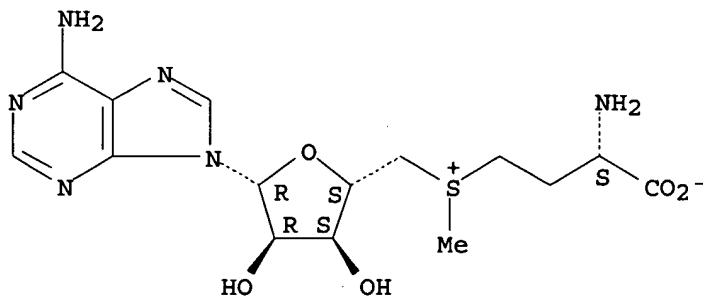
RN 13073-35-3 HCAPLUS
 CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 29908-03-0 HCAPLUS
 CN Adenosine, 5'-[[[(3S)-3-amino-3-carboxypropyl]methylsulfonio]-5'-deoxy-,
 inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:474604 HCAPLUS
 DOCUMENT NUMBER: 136:210154
 TITLE: Round window membrane delivery of L-methionine
 provides protection from cisplatin ototoxicity
 without compromising chemotherapeutic
 efficacy

AUTHOR(S): Li, Geming; Frenz, Dorothy A.; Brahmblatt, Sapna; Feghali, Joseph G.; Ruben, Robert J.; Berggren, Diana; Arezzo, Joseph; Van De Water, Thomas R.
 CORPORATE SOURCE: Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY, USA
 SOURCE: Neurotoxicology (2001), 22(2), 163-176
 CODEN: NRTXDN; ISSN: 0161-813X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Cisplatin (cis-diamminedichloroplatinum(II) (CDDP)) is a widely used, highly effective, oncolytic agent that has serious **ototoxic** side-effects. To test the effectiveness of local delivery of L-methionine (L-Met) as an otoprotective agent against CDDP **ototoxicity**, we used a rat model of a highly metastatic breast cancer tumor, i.e. Fisher 344 rats implanted with MTLn3 breast cancer cells. Four exptl. groups were evaluated - I: **untreated**; II: CDDP-treated (three dosages); III: systemically-delivered L-Met + CDDP-treated; IV: locally delivered L-Met + CDDP-treated. The integrity of the outer hair cells (OHCs) was determined using SEM; **hearing** was assessed by recording auditory brainstem responses (ABRs) at multiple frequencies. The **chemotherapeutic** effectiveness of CDDP was quantified by measuring changes in tumor mass and the presence of tumor metastasis. L-Met provided otoprotection of the OHCs against CDDP toxicity in the cochleae of rats following either systemic (III) or local (IV) administration. The ABRs were unchanged in each of the L-Met protection Groups (III and IV) and in the **untreated** animals of Group I. **Treatment** with CDDP only (II) induced significant **hearing** losses at both 16 and 18 kHz when compared to ABRs of **untreated** rats(I). CDDP was effective in **controlling** the MTLn3 initiated breast cancer tumors in the CDDP-treated (II) and the local L-Met protection, CDDP-treated (IV) Groups. In contrast, the tumors in the systemic L-Met protection, CDDP-treated Group (III) were not **controlled** by the CDDP **treatment** regime. This study demonstrates that local delivery of L-Met to the scala tympani of the cochlea via the round window membrane (IV) provides effective protection against CDDP **ototoxicity** without compromising its ability to **control** a highly metastatic form of cancer.

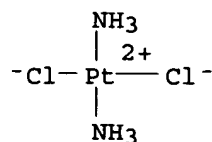
IT 15663-27-1, Cisplatin

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(round window membrane delivery of L-methionine provides protection from cisplatin **ototoxicity** without compromising **chemotherapeutic** efficacy)

RN 15663-27-1 HCAPLUS

CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



IT 63-68-3, L-Methionine, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

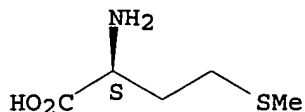
(round window membrane delivery of L-methionine provides

protection from cisplatin ototoxicity without compromising
chemotherapeutic efficacy)

RN 63-68-3 HCAPLUS

CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:338742 HCAPLUS

DOCUMENT NUMBER: 134:352782

TITLE: Oligomers and oligomeric segments of α -hydroxy
carboxylic acids and α -amino acids and uses in
improving bioavailability of nutrition supplement for
ruminants

INVENTOR(S): Lorbert, Stephen J.; Schasteen, Charles S.; Nam, Paul
K. S.; Forciniti, Daniel; Rajesh, Mathur P.; Kapila,
Shubhender

PATENT ASSIGNEE(S): Novus International, Inc., USA

SOURCE: PCT Int. Appl., 116 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032906	A2	20010510	WO 2000-US29897	20001030
WO 2001032906	A3	20020214		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1224318	A2	20020724	EP 2000-976719	20001030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.:			US 1999-162725P	P 19991029
			WO 2000-US29897	W 20001030

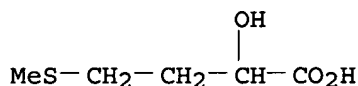
OTHER SOURCE(S): MARPAT 134:352782

AB The invention is relates to the enzymic synthesis and composition of
 α -hydroxy carboxylic acid and α -amino acid or peptide
co-oligomers wherein a residue of the α -hydroxy carboxylic acid is
linked to a residue of the α -amino acid or peptide by an amide
linkage. Proteolytic enzyme papain catalyzes co-oligomerization
of the α -hydroxy carboxylic acid and α -amino acid. The degree
and distribution of oligomerization varies upon the type and concns. of

different reaction mixts. utilized and upon the length of allowed reaction time. The present invention is further directed to a process for the preparation of an oligomer. The process comprises preparing a mixture containing (i) an

enzyme, (ii) an α -hydroxycarboxylic acid and (iii) an α -amino acid or a peptide oligomer. The α -hydroxy carboxylic acid and the α -amino acid each are present in the mixture as a free acid, acid halide, amide, ester or anhydride independently of the other. The process further comprises forming an amide linkage between the residue of the α -hydroxy carboxylic acid and the residue of the α -amino acid or the peptide oligomer. The resultant oligomers may be provided to ruminants as bioavailable amino acid supplements that are **resistant** to degradation in the rumen.

IT 583-91-5, 2-Hydroxy-4-(methylthio)butyric acid
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (oligomers and oligomeric segments of α -hydroxy carboxylic acids and α -amino acids and uses in improving bioavailability of nutrition supplement for ruminants)
 RN 583-91-5 HCAPLUS
 CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:664545 HCAPLUS

DOCUMENT NUMBER: 134:55978

TITLE: Effects of DL-methionine hydroxyanalogue (MHA) or DL-methionine (DL-Met) on N-retention in broiler chickens and pigs. [Erratum to document cited in CA132:207304]

AUTHOR(S): Romer, Andrea; Abel, Hj.

CORPORATE SOURCE: Institut fur Tierphysiologie und Tierernahrung, Gottingen, 37077, Germany

SOURCE: Animal Feed Science and Technology (2000), 83(3-4), 325

CODEN: AFSTDH; ISSN: 0377-8401

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

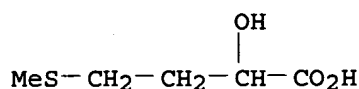
AB The reference to Walz and Pallauf (1996) was mistakenly cited in Section 4, page 301, line 9. The correct paragraph should read as follows: "As in broiler chickens there were also no differences in the effects of the two methionine sources on weight gain and feeding conversion ratios in pigs. This result confirms **earlier** studies (Chung and Baker, 1992; Reifsnnyder et al., 1984), reporting equal effects of DL-Met and DL-MHA on growth performance in pigs."

IT 583-91-5, Alimet

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
 (dietary DL-methionine hydroxy analog and DL-methionine effects on N-retention in broiler chickens and pigs (Erratum))

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:249071 HCAPLUS

DOCUMENT NUMBER: 130:262147

TITLE: Use of D-methionine or other
methionine compound to reduce the toxicity of
ototoxic drugs, noise, and radiation

INVENTOR(S): Campbell, Kathleen C. M.

PATENT ASSIGNEE(S): Southern Illinois University, USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917765	A1	19990415	WO 1998-US6960	19980408
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6187817	B1	20010213	US 1997-942845	19971002
CA 2303901	AA	19990415	CA 1998-2303901	19980408
AU 9869568	A1	19990427	AU 1998-69568	19980408
AU 753039	B2	20021003		
EP 1019036	A1	20000719	EP 1998-915362	19980408
EP 1019036	B1	20030625		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518499	T2	20011016	JP 2000-514636	19980408
AT 243511	E	20030715	AT 1998-915362	19980408
PT 1019036	T	20031128	PT 1998-915362	19980408
ES 2202834	T3	20040401	ES 1998-915362	19980408
PRIORITY APPLN. INFO.:			US 1997-942845	A 19971002
			US 1996-27750P	P 19961003
			WO 1998-US6960	W 19980408

OTHER SOURCE(S): MARPAT 130:262147

AB **Methods of preventing or reducing hearing or balance loss, damage to ear cells, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and prolonging survival in patients undergoing treatment with therapeutically effective amts. of platinum-containing chemotherapeutic agents, e.g. cisplatin, are provided. Methods are also provided for preventing or reducing such symptoms in patients undergoing treatment with loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, and quinidine, or those who have been exposed to toxic levels of noise or radiation. These methods comprise administering an**

effective amount of a **methionine** protective agent, e.g. D-**methionine**, prior to, simultaneously with, or subsequently to administration of the **platinum**-containing **chemotherapeutic** agent, loop diuretic agent, etc., or exposure to noise or radiation. Combinations of these time periods can also be employed.

IT 7439-89-6, Iron, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chelating agents; **methionine** compds. to reduce toxicity of
ototoxic drugs, noise, and radiation)

RN 7439-89-6 HCAPLUS

CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

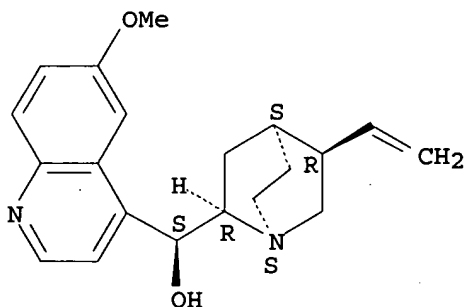
IT 56-54-2, Quinidine 130-95-0, Quinine 15663-27-1
, Cisplatin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**methionine** compds. to reduce toxicity of **ototoxic**
drugs, noise, and radiation)

RN 56-54-2 HCAPLUS

CN Cinchonan-9-ol, 6'-methoxy-, (9S)- (9CI) (CA INDEX NAME)

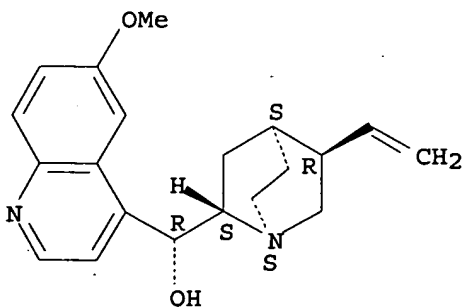
Absolute stereochemistry. Rotation (+).



RN 130-95-0 HCAPLUS

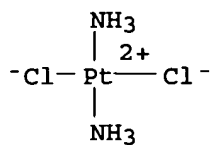
CN Cinchonan-9-ol, 6'-methoxy-, (8α,9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 15663-27-1 HCAPLUS

CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



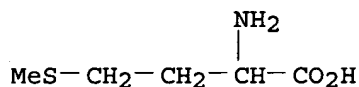
IT 59-51-8, Methionine 59-51-8D,
Methionine, compds. 63-68-3, L-Methionine,
biological studies 63-68-3D, L-Methionine, derivs.,
biological studies 348-67-4, D-Methionine
348-67-4D, D-Methionine, derivs. 502-83-0,
Methioninol 1319-79-5 13073-35-3, Ethionine
29908-03-0, S-Adenosyl-L-
methionine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methionine compds. to reduce toxicity of ototoxic drugs, noise, and radiation)

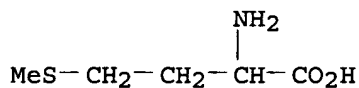
RN 59-51-8 HCAPLUS

CN Methionine (9CI) (CA INDEX NAME)



RN 59-51-8 HCAPLUS

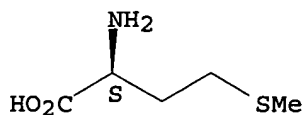
CN Methionine (9CI) (CA INDEX NAME)



RN 63-68-3 HCAPLUS

CN L-Methionine (9CI) (CA INDEX NAME)

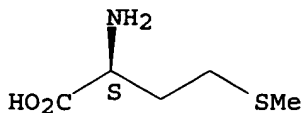
Absolute stereochemistry.



RN 63-68-3 HCAPLUS

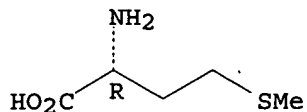
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



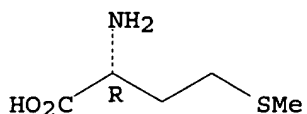
RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

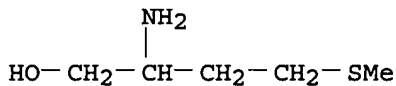


RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

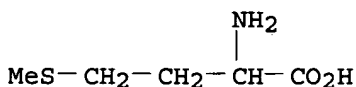
Absolute stereochemistry. Rotation (+).



RN 502-83-0 HCAPLUS
CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)



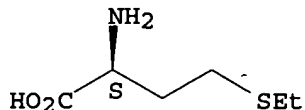
RN 1319-79-5 HCAPLUS
CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)



D1-OH

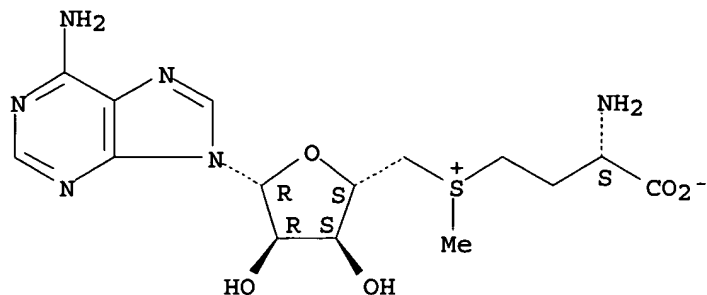
RN 13073-35-3 HCAPLUS
CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 29908-03-0 HCAPLUS
CN Adenosine, 5'-[[(3S)-3-amino-3-carboxypropyl]methylsulfonio]-5'-deoxy-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:219707 HCAPLUS

DOCUMENT NUMBER: 128:290226

TITLE: **Therapeutic use of a methionine compound, such as D-methionine, to reduce the toxicity of platinum-containing antitumor compounds**

INVENTOR(S): Campbell, Kathleen C. M.

PATENT ASSIGNEE(S): Southern Illinois University, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814182	A1	19980409	WO 1997-US18114	19971002
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2265983	AA	19980409	CA 1997-2265983	19971002
CA 2265983	C	20031223		
AU 9748957	A1	19980424	AU 1997-48957	19971002
AU 726392	B2	20001109		
EP 930877	A1	19990728	EP 1997-911634	19971002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001501626	T2	20010206	JP 1998-516973	19971002
PRIORITY APPLN. INFO.:			US 1996-27750P	P 19961003
			WO 1997-US18114	W 19971002

OTHER SOURCE(S): MARPAT 128:290226

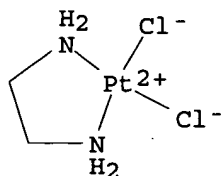
AB **Methods** are provided for **preventing** or **reducing** **hearing** or **balance loss**, **damage to ear cells**, **weight loss**, **gastrointestinal toxicity**, **neurotoxicity**, **alopecia**, and for **prolonging survival in patients undergoing treatment with**

therapeutically effective amts. of **platinum**-containing **chemotherapeutic** agents, e.g. cisplatin, are provided. These **methods** comprise administering an effective amount of a **methionine** protective agent, e.g. D-**methionine**, prior to, simultaneously with, or subsequently to administration of the **platinum**-containing **chemotherapeutic** agent. Combinations of these time periods can also be employed.

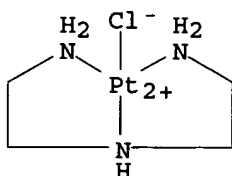
IT 7440-06-4D, **Platinum**, compds., biological studies
 14096-51-6, Dichloro(ethylenediamine) **platinum** (II)
 14215-58-8 14913-33-8 15663-27-1
 20115-64-4 38780-43-7 41575-93-3
 41575-94-4 62928-11-4, Iproplatin 64363-09-3
 67254-31-3 74790-08-2, Spiroplatin 88483-99-2
 114579-59-8 141610-50-6 149055-58-3
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methionine compound for reduction of toxicity of **platinum**-containing antitumor compds.)
 RN 7440-06-4 HCAPLUS
 CN Platinum (8CI, 9CI) (CA INDEX NAME)

Pt

RN 14096-51-6 HCAPLUS
 CN Platinum, dichloro(1,2-ethanediamine-κN,κN')-, (SP-4-2)- (9CI)
 (CA INDEX NAME)

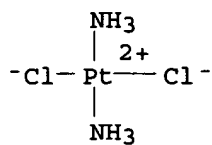


RN 14215-58-8 HCAPLUS
 CN Platinum(1+), [N-[2-(amino-κN)ethyl]-1,2-ethanediamine-κN,κN']chloro-, chloride, (SP-4-2)- (9CI) (CA INDEX NAME)



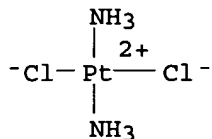
● Cl⁻

RN 14913-33-8 HCAPLUS
 CN Platinum, diamminedichloro-, (SP-4-1)- (9CI) (CA INDEX NAME)



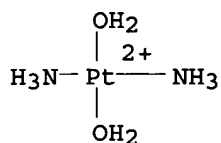
RN 15663-27-1 HCAPLUS

CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



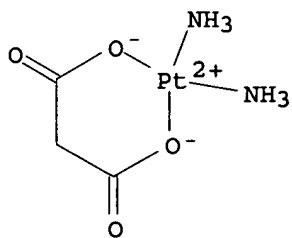
RN 20115-64-4 HCAPLUS

CN Platinum(2+), diamminediaqua-, (SP-4-2)- (9CI) (CA INDEX NAME)



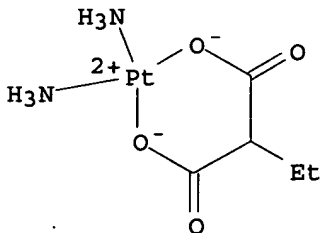
RN 38780-43-7 HCAPLUS

CN Platinum, diammine[propanedioato(2-)-κO1,κO3]-, (SP-4-2)- (9CI) (CA INDEX NAME)

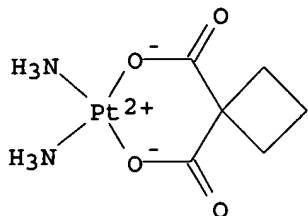


RN 41575-93-3 HCAPLUS

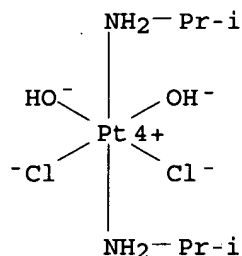
CN Platinum, diammine[ethylpropanedioato(2-)-κO1,κO3]-, (SP-4-2)- (9CI) (CA INDEX NAME)



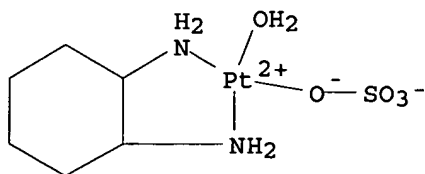
RN 41575-94-4 HCAPLUS

CN Platinum, diammine[1,1-cyclobutanedi(carboxylato- κ O) (2-)]-,
(SP-4-2) - (9CI) (CA INDEX NAME)

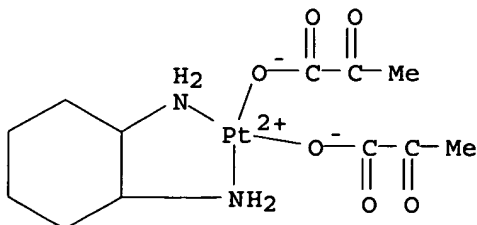
RN 62928-11-4 HCAPLUS

CN Platinum, dichlorodihydroxybis(2-propanamine)-, (OC-6-33) - (9CI) (CA
INDEX NAME)

RN 64363-09-3 HCAPLUS

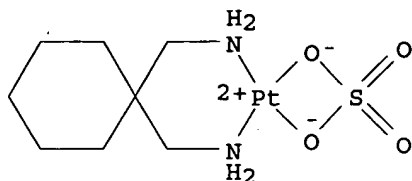
CN Platinum, aqua(1,2-cyclohexanediamine- κ N, κ N') [sulfato(2-)-
 κ O]-, (SP-4-3) - (9CI) (CA INDEX NAME)

RN 67254-31-3 HCAPLUS

CN Platinum, (1,2-cyclohexanediamine- κ N, κ N') bis(2-oxopropanoato-
 κ O)-, (SP-4-2) - (9CI) (CA INDEX NAME)

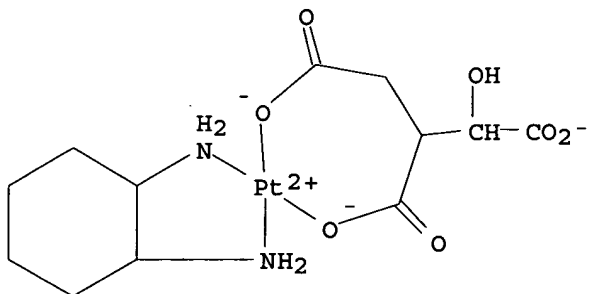
RN 74790-08-2 HCAPLUS

CN Platinum, (1,1-cyclohexanedimethanamine- $\kappa N, \kappa N'$) [sulfato(2-)- $\kappa O, \kappa O'$]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 88483-99-2 HCAPLUS

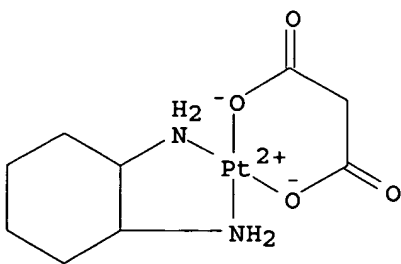
CN Platinate(1-), [3-(carboxy- κO)-2,3-dideoxypentatarato(3-)- $\kappa O1$] (1,2-cyclohexanediamine- $\kappa N, \kappa N'$)-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



● H⁺

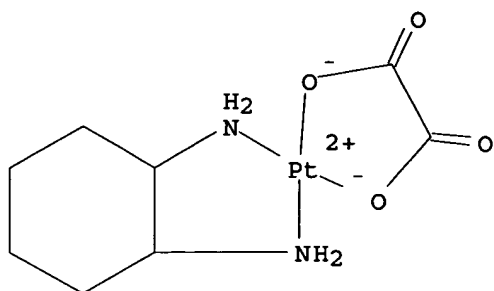
RN 114579-59-8 HCAPLUS

CN Platinum, (1,2-cyclohexanediamine- $\kappa N, \kappa N'$) [propanedioato(2-)- $\kappa O1, \kappa O3$]-, (SP-4-2)- (9CI) (CA INDEX NAME)

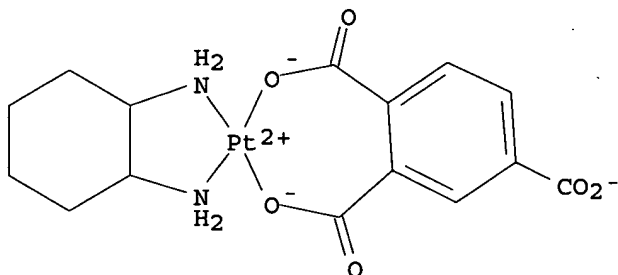


RN 141610-50-6 HCAPLUS

CN Platinum, (1,2-cyclohexanediamine- $\kappa N, \kappa N'$) [ethanedioato(2-)- $\kappa O1, \kappa O2$]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 149055-58-3 HCAPLUS
 CN Platinate(1-), [1,2,4-benzenetricarboxylato(3-)-κO1,κO2] (1,2-cyclohexanediamine-κN,κN')-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)

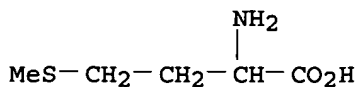


● H⁺

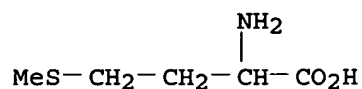
IT 59-51-8, **Methionine** 59-51-8D,
Methionine, derivs. 63-68-3, L-**Methionine**,
 biological studies 348-67-4, D-**Methionine**
 502-83-0, Methioninol 1319-79-5 13073-35-3,
 Ethionine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**methionine** compound for reduction of toxicity of **platinum** -containing antitumor compds.)

RN 59-51-8 HCAPLUS
 CN Methionine (9CI) (CA INDEX NAME)

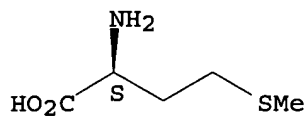


RN 59-51-8 HCAPLUS
 CN Methionine (9CI) (CA INDEX NAME)



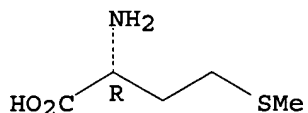
RN 63-68-3 HCAPLUS
CN L-Methionine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

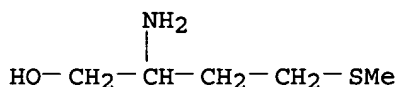


RN 348-67-4 HCAPLUS
CN D-Methionine (9CI) (CA INDEX NAME)

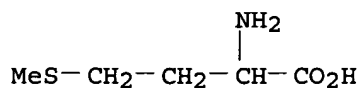
Absolute stereochemistry. Rotation (+).



RN 502-83-0 HCAPLUS
CN 1-Butanol, 2-amino-4-(methylthio)- (7CI, 8CI, 9CI) (CA INDEX NAME)



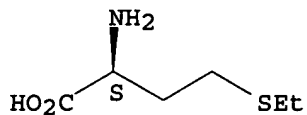
RN 1319-79-5 HCAPLUS
CN L-Methionine, hydroxy- (9CI) (CA INDEX NAME)



D1-OH

RN 13073-35-3 HCAPLUS
CN L-Homocysteine, S-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:177782 HCAPLUS

DOCUMENT NUMBER: 128:269942

TITLE: The relative effectiveness of 2-hydroxy-4-(methylthio)butanoic acid and DL-methionine in young swine

AUTHOR(S): Knight, C. D.; Atwell, C. A.; Wuelling, C. W.; Ivey, F. J.; Dibner, J. J.

CORPORATE SOURCE: Novus International, Inc., St. Charles, MO, 63304, USA

SOURCE: Journal of Animal Science (1998), 76(3), 781-787

CODEN: JANSAG; ISSN: 0021-8812

PUBLISHER: American Society of Animal Science

DOCUMENT TYPE: Journal

LANGUAGE: English

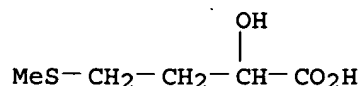
AB We compared the nutritional effectiveness of 2-hydroxy-4-(methylthio)butanoic acid (HMB) and DL-methionine (DLM) as sources of L-methionine in methionine-deficient primary cultures of pig liver cells and methionine-deficient early-weaned pigs. Viable hepatocytes were obtained from minced pig liver and maintained in a high d., differentiated, non-proliferation cell culture system. The culture medium was supplemented with HMB, DLM, or L-methionine, and the cells were pulse-dosed with L-[U-14C]leucine for 24 h to determine the level of protein synthesis. Leucine incorporation per mg of protein indicated a 6-8-fold increase in protein synthesis with methionine levels 5-10 μ M, regardless of the source of methionine. Two 24-pen replicate methionine dose titrns. were conducted with 95 early-weaned com. crossbred piglets. The pelleted corn, dried whey, and porcine blood plasma basal diet contained 1.5% lysine, 0.23% methionine, and 0.48% cystine, and was supplemented with 0, 0.05, or 0.10% methionine activity as DLM or HMB for 21 d. There was a 134, 104, and 61% increase in the cumulative average daily gain for each successive week of the study with a 30 and 19% improvement in the feed/gain ratio after 7 and 14 d. The growth performance due to the source of methionine did not differ and the slope ratio potency detns. (gain vs. intake of methionine source) of HMB vs. DLM indicated a 119, 111, and 95% relative activity for cumulative weekly performance. Thus, HMB and DLM may provide equimolar levels of methionine activity in swine.

IT 583-91-5, Alimet

RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(DL-methionine and 2-hydroxy-4-(methylthio)butanoic acid nutritional effectiveness in piglets)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:589425 HCAPLUS

DOCUMENT NUMBER: 127:257225

TITLE: Stereoselective peripheral sensory neurotoxicity of

diaminocyclohexane **platinum** enantiomers
related to ormaplatin and oxaliplatin
AUTHOR(S): Screnci, D.; Er, H. M.; Hambley, T. W.; Galettis, P.;
Brouwer, W.; Mckeage, M. J.
CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology,
The University of Auckland School of Medicine,
Auckland, N. Z.
SOURCE: British Journal of Cancer (1997), 76(4), 502-510
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The diaminocyclohexane **platinum** (Pt(DACH)) derivs.
ormaplatin and oxaliplatin have caused severe and dose-limiting peripheral
sensory neurotoxicity in a clin. trial. We hypothesized that this
toxicity could vary in relation to the biotransformation and stereochem.
of these Pt(DACH) derivs. We prepared pure R,R and S,S
enantiomers of ormaplatin (Pt(DACH)Cl4), oxaliplatin (Pt
(DACH)oxalato) and their metabolites (Pt(DACH)Cl2 and Pt
(DACH)methionine) and assessed their peripheral sensory
neurotoxicity and tissue distribution in the rat and in vitro **anti**
-tumor activity in **human** ovarian carcinoma cell lines.
The R,R enantiomers of Pt(DACH)Cl4, Pt(DACH)oxalato
and Pt(DACH)Cl2, induced peripheral sensory neurotoxicity at
significantly lower cumulative doses (18 ± 5.7 vs 32 ± 2.3 μ mol
kg⁻¹; $P < 0.01$) and at **earlier** times (4 ± 1 vs 6.7 ± 0.6 wk;
 $P = 0.016$) during repeat-dose **treatment** than the S,S enantiomers.
Pt(DACH)methionine enantiomers showed no biol. activity.
There was no difference between Pt(DACH) enantiomers in the
platinum concentration in sciatic nerve, dorsal root ganglia, spinal
cord, brain or blood at the end of each experiment. Three **human**
ovarian carcinoma cell lines (41M, 41McisR and SKOV-3) showed no (or
inconsistent) chiral discrimination in their sensitivity to Pt
(DACH) enantiomers, whereas two cell lines (CH-1 and CH-1cisR) showed
modest enantiomeric selectivity favoring the R,R isomer (more active). In
conclusion, Pt(DACH) derivs. exhibit enantiomeric-selective
peripheral sensory neurotoxicity during repeated dosing in rats favoring
S,S isomers (less neurotoxic). They exhibited less chiral discrimination
in their accumulation within peripheral nerves and in vitro **anti**
-tumor activity.

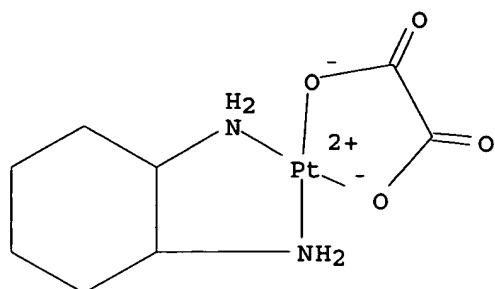
IT 61758-77-8 61825-94-3 61848-62-2
61848-66-6 96392-95-9 96392-96-0
195888-77-8 196108-97-1

RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC
(Process)

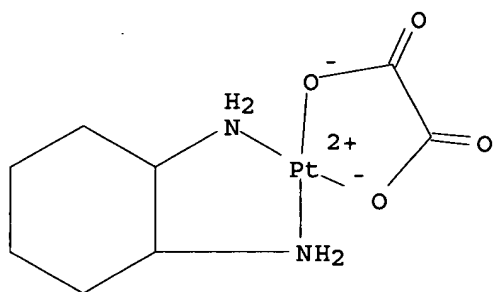
(stereoselective peripheral sensory neurotoxicity of diaminocyclohexane
platinum enantiomers related to ormaplatin and oxaliplatin)

RN 61758-77-8 HCAPLUS

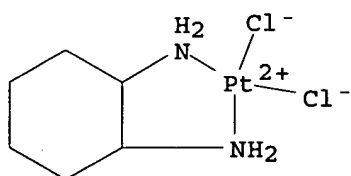
CN Platinum, [(1S,2S)-1,2-cyclohexanediamine-κN,κN'] [ethanedioato
(2-)-κO1,κO2]- (9CI) (CA INDEX NAME)



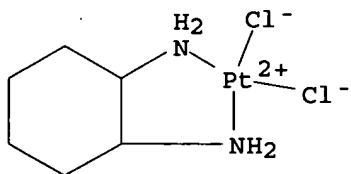
RN 61825-94-3 HCAPLUS
 CN Platinum, [(1R,2R)-1,2-cyclohexanediamine-κN,κN'] [ethanedioato
 (2-)-κO1,κO2]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 61848-62-2 HCAPLUS
 CN Platinum, dichloro[(1S,2S)-1,2-cyclohexanediamine-κN,κN']-,
 (SP-4-2)- (9CI) (CA INDEX NAME)

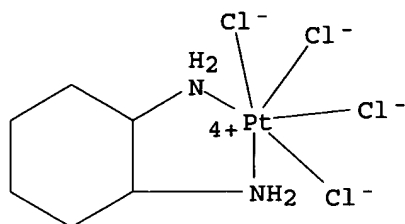


RN 61848-66-6 HCAPLUS
 CN Platinum, dichloro[(1R,2R)-1,2-cyclohexanediamine-κN,κN']-,
 (SP-4-2)- (9CI) (CA INDEX NAME)

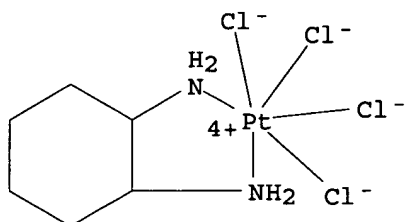


RN 96392-95-9 HCAPLUS
 CN Platinum, tetrachloro[(1S,2S)-1,2-cyclohexanediamine-κN,κN']-,

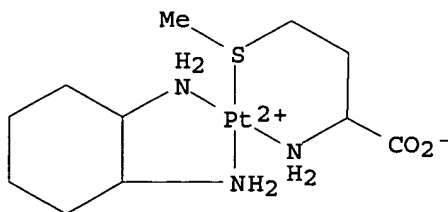
(OC-6-22) - (9CI) (CA INDEX NAME)



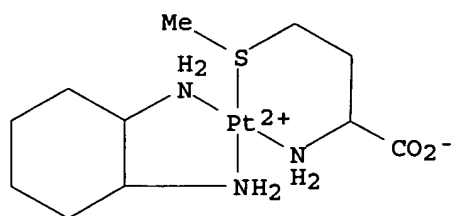
RN 96392-96-0 HCAPLUS
 CN Platinum, tetrachloro[(1R,2R)-1,2-cyclohexanediamine-κN,κN']-,
 (OC-6-22) - (9CI) (CA INDEX NAME)



RN 195888-77-8 HCAPLUS
 CN Platinum(1+), [(1R,2R)-1,2-cyclohexanediamine-κN,κN'] (L-methioninato-κN,κS)-, monohydrogen, (SP-4-3) - (9CI) (CA INDEX NAME)

● H⁺

RN 196108-97-1 HCAPLUS
 CN Platinum(1+), (1,2-cyclohexanediamine-κN,κN') (L-methioninato-κN,κS)-, monohydrogen, [SP-4-3-(1S-trans)] - (9CI) (CA INDEX NAME)



● H⁺

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:261094 HCAPLUS

DOCUMENT NUMBER: 126:311874

TITLE: **Treatment with inhibitors of polyamine biosynthesis**, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**

AUTHOR(S): Desiderio, M. A.; Bergamaschi, D.; Mascellani, E.; De Feudis, P.; Erba, E.; D'incalci, M.

CORPORATE SOURCE: Istituto di Patologia Generale, Universita degli Studi di Milano and Centro di studio sulla Patologia Cellulare, CNR, Milan, Italy

SOURCE: British Journal of Cancer (1997), 75(7), 1028-1034

CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Inhibitors** of ornithine decarboxylase (ODC), such as α -difluoromethylornithine (DFMO), may influence the cytotoxicity of **anti-tumor** agents that interact with DNA. Intracellular levels of putrescine and spermidine were markedly reduced by ODC **inhibitors** while the level of spermine, which is the main polyamine in nuclei, was unchanged. By combining a novel **inhibitor** of ODC, such as (2R, 5R)-6-heptyne-2,5-diamine (MDL 72.175, MAP), with an **inhibitor** of S-adenosylmethionine decarboxylase (SAMDC), such as 5'-[[(Z)-4-aminobut-2-enyl]methylamino]-5'-deoxyadenosine (MDL 73.811, AbeAdo), spermine was selectively depleted in a **human** ovarian cancer cell line OVCAR-3 (i.e. spermine became almost undetectable whereas the levels of spermidine and putrescine were not affected). The depletion of spermine blocked DNA synthesis with a consequent accumulation of cells in the G1 phase of the cell cycle. **Pretreatment** with MAP plus AbeAdo did not change the cytotoxicity of alkylating agents, such as L-phenylalanine mustard (L-PAM), 1,4-bis (2-chloroethyl)-1, 4-diazabicyclo-[2.2.1] heptane diperchlorate (DABIS), 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU), **cis-diamminedichloroplatinum** (II) (cis-DDP), N-deformyl-N-[4-N,N,N-bis (2-chloroethylamino)benzoyl] (tallimustine) or CC-1065, whereas it markedly reduced the cytotoxicity of DNA topoisomerase II **inhibitors**, such as doxorubicin (DX) and 4'-demethylepipodophyllotoxin-5-(4,6-O)-ethylidene- β -D-glycopyranoside (VP-16). The addition of spermine before drug **treatment** restored

the sensitivity to the DNA topoisomerase II **inhibitors**, thus indicating that the reduced effect was related to the intracellular spermine level. The reason for the reduction in cytotoxicity is unclear, but it does not appear to be related to a cell cycle effect or to a decrease in the intracellular level of DNA topoisomerase II. Drugs that modify polyamine biosynthesis are under **early** clin. development as potential new **anti-tumor** agents. These findings illustrate the need for caution in combining such drugs with DNA topoisomerase II **inhibitors**.

IT 9024-60-6, Ornithine decarboxylase 9036-20-8, S-Adenosylmethionine decarboxylase 142805-56-9, DNA topoisomerase II

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**inhibitors; treatment with inhibitors of** polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**)

RN 9024-60-6 HCAPLUS

CN Decarboxylase, ornithine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9036-20-8 HCAPLUS

CN Decarboxylase, adenosylmethionine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 142805-56-9 HCAPLUS

CN Isomerase, deoxyribonucleate topo-, II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 148-82-3, L-Phenylalanine mustard 154-93-8, BCNU

1020-94-6 15663-27-1 23214-92-8, Doxorubicin

33419-42-0, VP-16 69866-21-3, CC-1065 88192-22-7

, MDL 72175 115308-98-0, Tallimustine 123642-27-3, MDL 73811

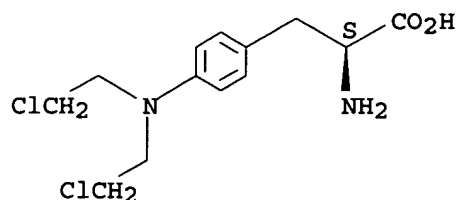
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**treatment with inhibitors of** polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II **inhibitors**)

RN 148-82-3 HCAPLUS

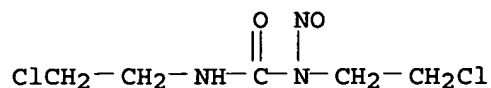
CN L-Phenylalanine, 4-[bis(2-chloroethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154-93-8 HCAPLUS

CN Urea, N,N'-bis(2-chloroethyl)-N-nitroso- (9CI) (CA INDEX NAME)



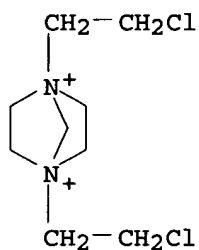
RN 1020-94-6 HCAPLUS

CN 1,4-Diazoniabicyclo[2.2.1]heptane, 1,4-bis(2-chloroethyl)-, diperchlorate
(8CI, 9CI) (CA INDEX NAME)

CM 1

CRN 21787-85-9

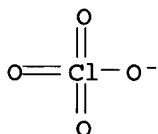
CMF C9 H18 Cl2 N2



CM 2

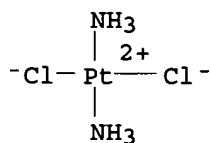
CRN 14797-73-0

CMF Cl O4



RN 15663-27-1 HCAPLUS

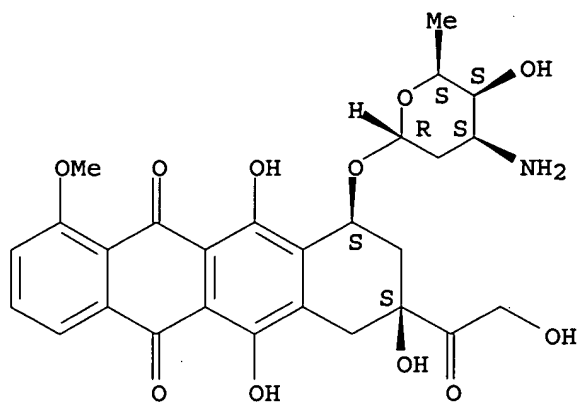
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 23214-92-8 HCAPLUS

CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy- α -L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

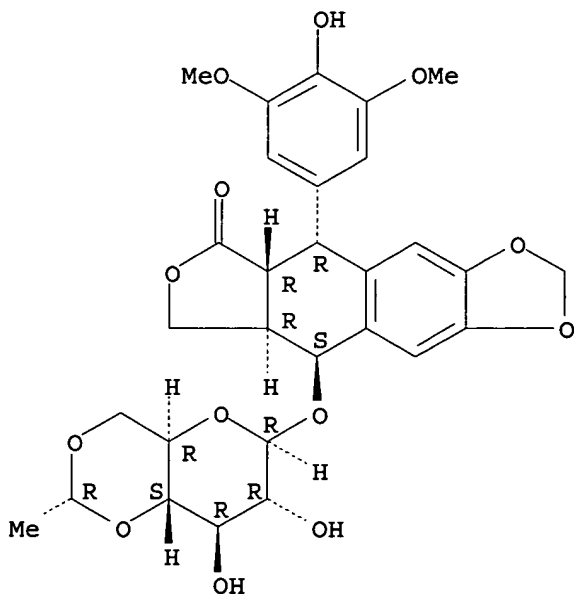
Absolute stereochemistry.



RN 33419-42-0 HCAPLUS

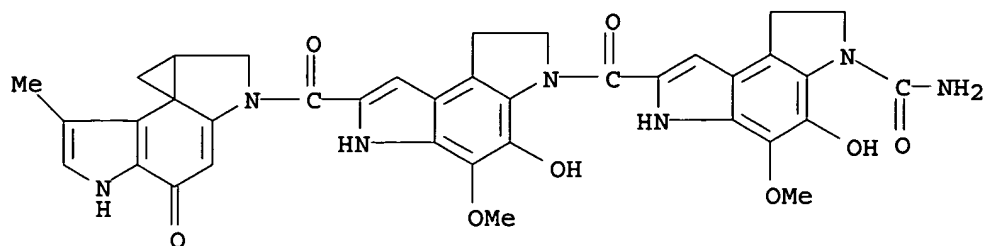
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[4,6-O-(1R)-ethylidene-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 69866-21-3 HCAPLUS

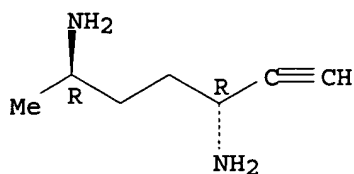
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxamide, 7-[[1,6-dihydro-4-hydroxy-5-methoxy-7-[(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl]carbonyl]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1,6-dihydro-4-hydroxy-5-methoxy-, (7bR,8aS)- (9CI) (CA INDEX NAME)



RN 88192-22-7 HCAPLUS

CN 6-Heptyne-2,5-diamine, (2R,5R) - (9CI) (CA INDEX NAME)

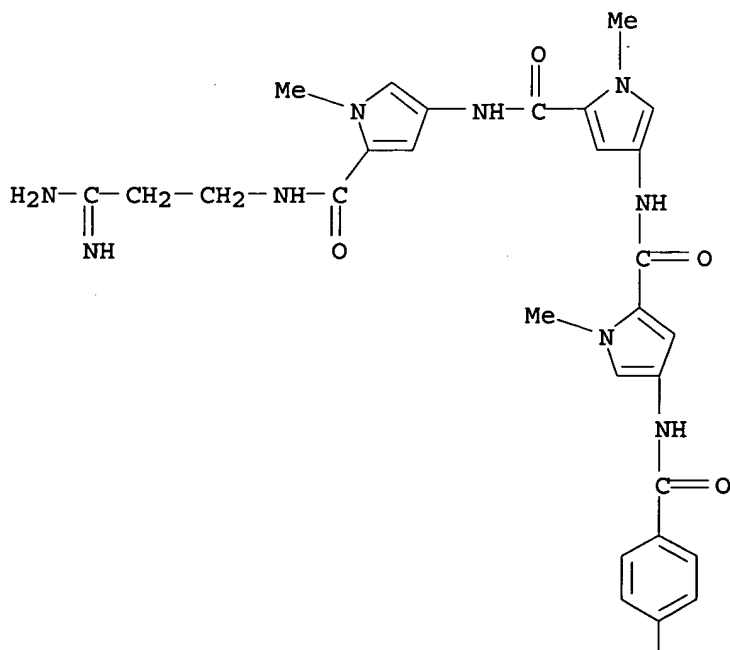
Absolute stereochemistry.



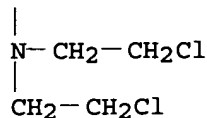
RN 115308-98-0 HCAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[[(3-amino-3-iminopropyl) amino] carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[[4-[bis(2-chloroethyl) amino] benzoyl] amino]-1-methyl-1H-pyrrol-2-yl] carbonyl] amino]-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

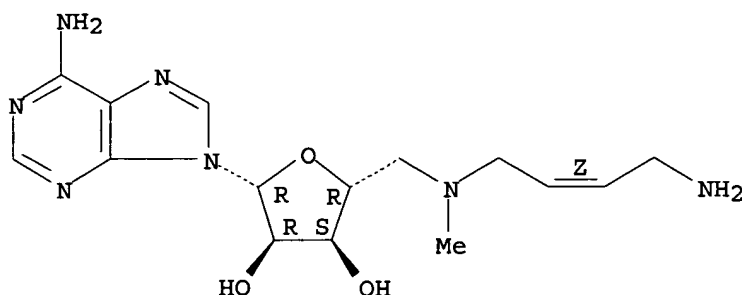


PAGE 2-A

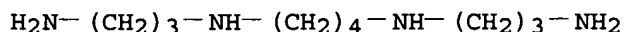


RN 123642-27-3 HCAPLUS
 CN Adenosine, 5'-[[(2Z)-4-amino-2-butenyl]methylamino]-5'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



IT 71-44-3, Spermine
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (treatment with inhibitors of polyamine biosynthesis, which selectively lower intracellular spermine, does not affect the activity of alkylating agents but antagonizes the cytotoxicity of DNA topoisomerase II inhibitors)
 RN 71-44-3 HCAPLUS
 CN 1,4-Butanediamine, N,N'-bis(3-aminopropyl)- (8CI, 9CI) (CA INDEX NAME)



L33 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1996:655958 HCAPLUS
 DOCUMENT NUMBER: 126:7060
 TITLE: Studies on metabolism of broilers by using 14C-labeled DL-methionine and DL-methionine hydroxy analog Ca-salt
 AUTHOR(S): Lingens, G.; Molnar, S.
 CORPORATE SOURCE: Institute Animal Physiology Animal Nutrition, University Goettingen, Goettingen, D-37077, Germany
 SOURCE: Archives of Animal Nutrition (1996), 49(2), 113-124
 CODEN: AANUET
 PUBLISHER: Harwood
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The incorporation of the growth-limiting DL-methionine (MET) into the body of 60-day-old male chickens was higher than that of the DL-methionine hydroxy analog (HM). Of the incorporated 14C, 17% was released in excrements and 15.8% in the expired air after MET feeding; and 4.4% was

released in excrements and 11.4% in the expired air after HM feeding. The incorporation of MET or HM in the digestive tract, blood, kidney, liver, gallbladder, lung, heart, spleen, and leg and breast muscles was also investigated.

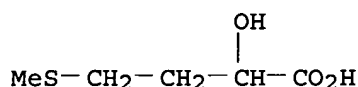
IT 583-91-5

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(metabolism of broilers studied by ¹⁴C-labeled DL-methionine and DL-methionine hydroxy analog Ca-salt)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:494118 HCAPLUS

DOCUMENT NUMBER: 119:94118

TITLE: Fatty acid salt preparations containing other biologically active materials for use as feed supplements

INVENTOR(S): Vinci, Alfredo; Lajoie, M. Stephen; Sweeney, Thomas F.; Cummings, Kenneth R.

PATENT ASSIGNEE(S): Church and Dwight Co., Inc., USA

SOURCE: PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9310669	A1	19930610	WO 1992-US7337	19920904
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9225774	A1	19930628	AU 1992-25774	19920904
EP 619706	A1	19941019	EP 1992-919798	19920904
EP 619706	B1	19991124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
BR 9206859	A	19960416	BR 1992-6859	19920904
AT 186817	E	19991215	AT 1992-919798	19920904
CA 2124925	C	20011002	CA 1992-2124925	19920904
US 5456927	A	19951010	US 1993-149305	19931109
WO 9512987	A1	19950518	WO 1994-US9137	19940822
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
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AU 9476315	A1	19950529	AU 1994-76315	19940822
PRIORITY APPLN. INFO.:			US 1991-802261	A 19911204
			US 1993-149305	19931109

US 1993-7013 19930121
 WO 1992-US7337 A 19920904
 WO 1994-US9137 W 19940822

AB The salts of C14-22 fatty acids for use as feed supplements for cattle are prepared with simultaneous incorporation of other feed supplements. By using the alkali earth metal salts of fatty acids, the fatty acids and the incorporated supplements have rumen bypass protection and so do not adversely affect rumen microflora. A series of feed supplements 35 were included in a stirred reaction mixture including palm oil fatty acids 700 , calcium oxide 100 and water 300 g. During the highly exothermic reaction nicotinic acid, methionine, lysine, or choline were broken down to a significant extent, but methionine hydroxy analog and nicotinamide were unaffected.

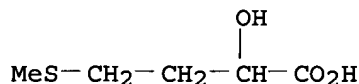
IT 583-91-5

RL: BIOL (Biological study)

(as feed supplement, rumen bypass-protected, preparation of fatty acid calcium salts in relation to)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:113544 HCAPLUS

DOCUMENT NUMBER: 110:113544

TITLE: Effect of days of lactation and methionine hydroxy analog on incorporation of plasma fatty acids into plasma triglycerides

AUTHOR(S): Pullen, David L.; Palmquist, D. L.; Emery, R. S.

CORPORATE SOURCE: Dep. Anim. Sci., Michigan State Univ., East Lansing, MI, 48824, USA

SOURCE: Journal of Dairy Science (1989), 72(1), 49-58

CODEN: JDSCAE; ISSN: 0022-0302

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cows were fed diets containing 0 or 30 g methionine hydroxy analog (I)/day starting 14 days prepartum. At .apprx.30 and 60 days postpartum, cows were continuously infused i.v. with 1-[14C]palmitic acid for 160 min to achieve steady-state labeling of plasma fatty acids and triglycerides. Turnover of fatty acids and transfer quotients for triglycerides and CO2 were 3.3 and 2.7 mmol/min; 13.0 and 10.0%; and 8.0 and 5.0%, for control and I, resp. Proportion of fatty acid turnover incorporated into triglycerides and CO2 were 14.0 and 15.0%; and 21.0 and 18.0, resp., for control and I. I increased 14C recovered in milk fat (52 vs. 36%). Plasma concentration of fatty acids, percent oxidized

to

CO2, and percent of CO2 from fatty acids decreased with increasing lactation days. Milk fat percent and yield, fatty acid turnover, and oxidation were pos. correlated with concentration of plasma fatty acids,

whereas

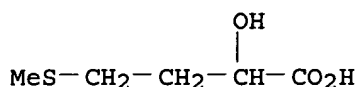
fatty acid incorporated into plasma triglyceride was neg. correlated with fatty acid concentration. Apparently, hepatic triglyceride secretion is not increased in early lactation; further, no effects of analog on lipid metabolism were detected.

IT 583-91-5, Methionine hydroxy analog

RL: BIOL (Biological study)
 (fatty acid metabolism and triglyceride formation by dairy cows in
 lactation response to, feeding experiment in relation to)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:438442 HCAPLUS

DOCUMENT NUMBER: 107:38442

TITLE: Effect of fasting and of methionine deficiency on
 L-methionine, DL-methionine and DL-2-hydroxy-4-
 methylthiobutanoic acid metabolism in broiler chicks

AUTHOR(S): Saunderson, C. Linda

CORPORATE SOURCE: Inst. Grassland Anim. Prod., AFRC, Roslin/Midlothian,
 EH25 9PS, UK

SOURCE: British Journal of Nutrition (1987), 57(3), 429-37
 CODEN: BJNUAV; ISSN: 0007-1145

DOCUMENT TYPE: Journal

LANGUAGE: English

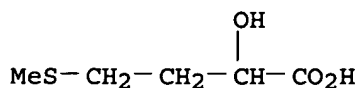
AB Metabolism of L-[1-14C]methionine, DL-[1-14C]methionine, and
 DL-[1-14C]2-hydroxy-4-methylthiobutanoic acid (DL-HMB) by broiler chicks
 which had been fasted overnight or given a methionine-deficient diet was
 compared with fed (**control**) birds. The excretion of 14C-labeled
 material, total 14CO₂ exhaled, 14C incorporation into tissue proteins, and
 the 14C-labeled material in HClO₄-soluble tissue fractions were measured 6 h
 after injection of the 14C-labeled materials. The incorporation of 14C
 into tissue proteins and the relative rates of conversion of D-methionine
 and DL-HMB to L-methionine in tissues under different nutritional regimens
 were compared using protein-bound 14C:protein-free 14C values. Fasted
 birds exhaled more 14CO₂ than **control** birds but excreted less
 14C, while methionine-deficient birds behaved very similarly to the
control animals in these respects. Fasted birds incorporated much
 less 14C into proteins of tissues other than liver and kidney from all 3
 labeled tracers. The values for protein-bound 14C:protein-free 14C were
 lower in all tissues. Methionine-deficient birds had similar levels of
 14C in tissue proteins but lower values for protein bound 14C:protein-free
 14C. Examination of the values for protein-bound 14C:protein-free 14C suggest
 that brain and probably liver tissues from fasted and methionine-deficient
 birds showed improved rates of conversion of D-methionine and DL-HMB to
 L-methionine compared with **control** animals.

IT 583-91-5

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (metabolism of, by broiler chicks, fasting and methionine deficiency effect
 on)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1986:144867 HCAPLUS

DOCUMENT NUMBER: 104:144867

TITLE: The occurrence of 4-methylthio-2-hydroxybutyrate in human urine

AUTHOR(S): Maartensson, Johannes

CORPORATE SOURCE: Dep. Clin. Chem., Univ. Hosp. Linköping, Linköping, S-581 85, Swed.

SOURCE: Analytical Biochemistry (1986), 154(1), 43-9

CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

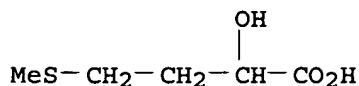
AB A method for determination of 4-methylthio-2-hydroxybutyrate and 4-methylthio-2-oxobutyrate in human urine was devised, based on methoxime formation of the keto acid and a clean-up procedure using the strong anion-exchange resin AG 2X8 and EtOAc extraction. After alkylation, the compds. were quantified by gas chromatog. using a flame photometric S-selective detector. Separation was done on a silanized glass column (6 ft) filled with 3% OV17 on Chromosorb WHP (100-200 mesh), with temps. of 220, 140, and 250° for injector, column, and detector, resp. The carrier gas was He. A normal urinary excretion of 0.14-0.25 mmol/mol creatinine and 0.07-0.22 mmol/mol creatinine of the α -hydroxy and α -keto acid, resp., was found, whereas a markedly elevated excretion of the hydroxy acid was noted in subjects with hypermethioninemia. The enzymic reduction of 4-methylthio-2-oxobutyric acid by lactate dehydrogenase:NAD⁺ oxidoreductase (EC 1.1.1.17) was also studied. The K_m and K_{eq} values for 4-methylthio-2-oxobutyrate were 1.41 mM and 0.92 + 108 M⁻¹. The V_{max} value of the enzyme at infinite concns. of the 2 substrates was 7.2 μ mol/s/ μ mol enzyme, which indicates low affinity and reduced catalytic activity compared to other known substrates of lactate dehydrogenase. The reaction product 4-methylthio-2-hydroxybutyrate was not inhibitory on the reaction. The M4 isoenzyme of lactate dehydrogenase (rabbit and pig muscle) had approx. 20% of the activity of the H4 isoenzyme (pig heart) for the substrate.

IT 583-91-5P

RL: ANT (Analyte); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(determination of, in human urine by gas chromatog. in health and hypermethioninemia)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1986:3567 HCAPLUS

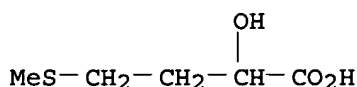
DOCUMENT NUMBER: 104:3567

TITLE: Comparative metabolism of L-methionine, DL-methionine and DL-2-hydroxy-4-methylthiobutanoic acid by broiler chicks

AUTHOR(S): Saunderson, C. Linda

CORPORATE SOURCE: Poult. Res. Cent., Agric. Food Res. Counc., Roslin,

EH25 9PS, UK
 SOURCE: British Journal of Nutrition (1985), 54(3), 621-33
 CODEN: BJNUAV; ISSN: 0007-1145
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Metabolism, in broiler chicks, of DL-2-hydroxy-4-methylthiobutanoic acid (DL-HMB), DL-methionine and L-methionine was compared in vivo using ¹⁴C-labeled tracers. The distribution of L-[1-¹⁴C]methionine and DL-[1-¹⁴C]HMB in the major body tissues was examined for 120 min after administration. The relative oxidation (¹⁴CO₂ exhaled), excretion, and incorporation into tissue protein of L-[1-¹⁴C]methionine, DL-[1-¹⁴C]methionine and DL-[1-¹⁴C]HMB were measured in fed birds. Tissue distribution of L-[1-¹⁴C]methionine and DL-[1-¹⁴C]HMB differed during 60-90 min following administration. The production of ¹⁴CO₂ from each of the tracers was similar, but excretion of ¹⁴C-labeled material was very different with the greatest excretion from DL-[1-¹⁴C]HMB and the least from L-[1-¹⁴C]methionine. The incorporation of ¹⁴C into tissue proteins varied with the tracer given and the tissue examined. Liver and kidney had equivalent incorporation from each of the tracers, whereas other tissues examined showed lower incorporation from DL-[1-¹⁴C]methionine and DL-[1-¹⁴C]HMB. Thus, DL-HMB, D-methionine, and L-methionine are metabolized differently in vivo and they are excreted in differing proportions. There is also a difference in the ability of each to act as a precursor for protein synthesis in tissues other than liver.
 IT 583-91-5
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (metabolism of, by chicken)
 RN 583-91-5 HCAPLUS
 CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1985:217690 HCAPLUS
 DOCUMENT NUMBER: 102:217690
 TITLE: Studies of metabolites in diarrheal stool specimens containing Shigella species by frequency-pulsed electron capture gas-liquid chromatography
 AUTHOR(S): Brooks, J. B.; Basta, M. T.; El Kholy, A. M.
 CORPORATE SOURCE: Div. Bacterial Dis., Cent. Infect. Dis., Atlanta, GA, 30333, USA
 SOURCE: Journal of Clinical Microbiology (1985), 21(4), 599-606
 CODEN: JCMIDW; ISSN: 0095-1137
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Diarrheal stool specimens and control stool specimens from Cairo, Egypt, were studied by frequency-pulsed electron capture gas chromatog. (FPEC-GLC). Cases involving S. sonnei, cases involving S. boydii, and cases involving S. flexneri were studied. The aqueous stools were centrifuged, extracted with organic solvents, and derivatized to form specific electron-capturing derivs. of carboxylic acids, alcs., hydroxy acids, and amines. Analyses were performed on high-resolution glass columns with an

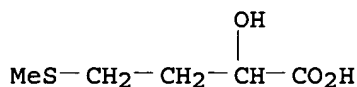
instrument equipped with an extremely sensitive electron capture detector that is specific for the detection of electron-capturing compds. The **diarrheal** stools studied had specific FPEC-GLC profiles and contained metabolic markers that readily distinguished between the *Shigella* species studied and *Escherichia coli* producing heat-stable or heat-labile enterotoxins. *S. sonnei* Stools contained hexanoic acid, 2-hydroxy-4-methylmethiobutyric acid, and some unidentified alcs. that distinguished this organism from other enteric pathogens. *S. boydii* Produced an acid that was unique for this species, and *S. flexneri* produced alcs. that could be used to distinguish between it and other enteric organisms. The FPEC-GLC profiles obtained during this study were also very different from those reported **earlier** for *Clostridium difficile* and rotavirus. This study presents further evidence that the selectivity and sensitivity of FPEC-GLC **techniques** can be used to rapidly identify causative agents of diarrhea and detect phsiol. changes that occur in the gut during the course of **diarrheal** illness.

IT 583-91-5

RL: ANT (Analyte); ANST (Analytical study)
(determination of, in feces of **humans** in diarrhea by gas chromatog.)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1981:478882 HCAPLUS

DOCUMENT NUMBER: 95:78882

TITLE: Influence of ration composition and energy balance on blood β -hydroxybutyrate (ketone) and plasma glucose concentrations of dairy cows in **early** lactation

AUTHOR(S): Herdt, T. H.; Stevens, J. B.; Linn, J.; Larson, V.

CORPORATE SOURCE: Dep. Large Anim. Clin. Sci., Univ. Minnesota, St. Paul, MN, 55108, USA

SOURCE: American Journal of Veterinary Research (1981), 42(7), 1177-80

CODEN: AJVRAH; ISSN: 0002-9645

DOCUMENT TYPE: Journal

LANGUAGE: English

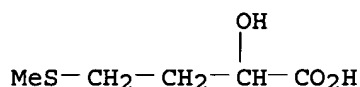
AB The effect of ratio composition, with respect to concentrate, crude protein, and

methionine hydroxy analog [583-91-5] content, on blood β -hydroxybutyrate [300-85-6] and plasma glucose [50-99-7] concns. was assessed in Holstein cows every 2 wk over the first 6 wk of lactation. The correlation of these metabolites with estimated energy balance, and the effects of these ration variables on this correlation were studied. High concentrate diets (60% of dry matter) compared with low concentrate diets (40% of dry

matter) increased mean plasma glucose values and reduced mean blood β -hydroxybutyrate concentration. Variation in crude protein and methionine hydroxy analog supplementation did not affect metabolite concentration. The correlations between blood β -hydroxybutyrate and energy balance and between plasma glucose and energy balance were weak and subject to the influence of variation in ration composition. Plasma glucose and blood

β -hydroxybutyrate concns. cannot be used as valid indicators of energy balance. However, it did appear that blood β -hydroxybutyrate might be used as an indicator of the relative glucogenic potential of dairy rations and that blood concns. of this metabolite could potentially be used to adjust factors in the ration which influence glucose availability to the cow.

IT 583-91-5
 RL: BIOL (Biological study)
 (blood β -hydroxybutyrate and plasma glucose of dairy cows in relation to dietary)
 RN 583-91-5 HCAPLUS
 CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1978:103738 HCAPLUS

DOCUMENT NUMBER: 88:103738

TITLE: The use of whole barley diets fortified with solutions of urea, minerals and vitamins for lambs

AUTHOR(S): Oerskov, E. R.; Grubb, D. A.

CORPORATE SOURCE: Rowett Res. Inst., Bucksburn/Aberdeen, UK

SOURCE: Animal Feed Science and Technology (1977), 2(4), 307-14

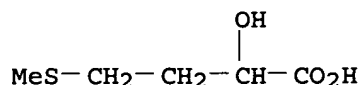
CODEN: AFSTDH; ISSN: 0377-8401

DOCUMENT TYPE: Journal

LANGUAGE: English

AB For 1 experiment 45 **early**-weaned lambs were given one of the following 5 diets from weaning to slaughter: (1) whole barley with urea [57-13-6], minerals, and vitamins added as a concentrated solution; (2) as diet (1) plus 4 g/kg of Na₂SO₄ in solution; (3) as diet (2) plus 1.2 g of methionine hydroxy analog (MHA) [583-91-5]/kg; (4) as diet (2) plus 2.5 mL of 40% CH₂O added per kg; (5) a **control** diet containing whole barley and 100 g/kg of a pelleted supplement based on fish meal. Growth rates (g/day) for the 5 **treatments** were 218,253,253,256, and 292. Addition of SO₄²⁻ significantly increased growth rate and food utilization while MHA had no effect; formalin **treatment** reduced digestibility and food utilization. In a 2nd experiment 58 lambs were used to study the effect of protein supplements for lambs weaned at various ages and wts. Diets similar to (2) and (5) from experiment (1) were used, while an intermediate diet (6) was made from an equal mixture of diets (2) and (5). As weaning age increased and as live weight at weaning increased, the difference in growth rate and food utilization between lambs receiving diet (2) and those receiving diets (5) and (6) decreased. It is suggested that for most sheep production systems in which concs. are used either as the sole feed or as supplements, simple fortification of whole grain with the necessary nutrients is all that is required to achieve optimum results.

IT 583-91-5
 RL: BIOL (Biological study)
 (feed experiment with, on lambs, barley in relation to)
 RN 583-91-5 HCAPLUS
 CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1978:5165 HCAPLUS

DOCUMENT NUMBER: 88:5165

TITLE: Methionine hydroxy analog in diets for lactating cows

AUTHOR(S): Bhargava, P. K.; Otterby, D. E.; Murphy, J. M.;
Donker, J. D.

CORPORATE SOURCE: Dep. Anim. Sci., Univ. Minnesota, St. Paul, MN, USA

SOURCE: Journal of Dairy Science (1977), 60(10), 1594-604

CODEN: JDSCAE; ISSN: 0022-0302

DOCUMENT TYPE: Journal

LANGUAGE: English

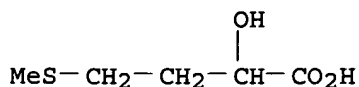
AB In 2 trials in consecutive years 47 and 50 lactating Holstein cows were assigned to grain mixts. that contained 0, 0.1, 0.2, and 0.3% methionine hydroxy analog [583-91-5]. Exptl. diets were offered to the cows beginning 2 wk prepartum, and collection of data was begun 4 days postpartum. Alfalfa hay and corn silage were fed ad libitum in a ratio of 1:1, dry basis. Milk fat test and yield were higher for cows supplemented with analog than for **controls** during **early** (4-116 days) lactation. Daily fiber intake was higher for cows fed 0.3% analog (2.2 kg) than for **controls** (1.9 kg) during **early** lactation in y 1 but not in y 2. Milk and solids-not-fat yields did not differ among **treatments**. Intakes of dry matter were not affected by **treatment**. From 117 to 256 days of lactation, there were no differences in yields of milk, fat, or solids-not-fat. Milk from cows maintained on the same **treatment** both y changed little in fat test from y 1 to y 2, but cows that were changed from high analog during y 1 to low during y 2 decreased 0.48 percentage units in test. Those changed from no analog to analog increased 0.34 percentage units in test, and those changes from low analog to high analog increased 0.23 percentage units. Methionine hydroxy analog appears to be a useful supplement for increasing fat test of cows fed relatively high concentrate diets.

IT 583-91-5

RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)
(feeding experiment with, on cows, milk fat in relation to)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1977:28736 HCAPLUS

DOCUMENT NUMBER: 86:28736

TITLE: Response to nonprotein nitrogen and sulfur sources by the **early**-weaned calf

AUTHOR(S): Winter, K. A.

CORPORATE SOURCE: Res. Stn., Agric. Canada, Charlottetown, PE, Can.

SOURCE: Canadian Journal of Animal Science (1976), 56(3),
567-72

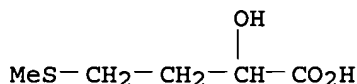
CODEN: CNJNAT; ISSN: 0008-3984

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Calves were used in 2 expts. to evaluate 2 nonprotein N sources and several S sources in calf starter rations. Experiment (1) compared urea [57-13-6] and biuret [108-19-0], with and without methionine hydroxy analog (MHA) [583-91-5], and S plus MHA; experiment (2) compared the effect of elemental S and Na₂SO₄ added to a urea-supplemented starter on calf response to these feeds. Performance of calves on the biuret-supplemented starters was reduced as compared with urea-supplemented starters. The addition of S or MHA to the NPN-supplemented starters did not affect animal performance. However, S did tend to improve performance of the urea-fed calves and had the reverse effect when biuret was fed, while MHA tended to depress performance when urea was fed. In the 2nd experiment, the addition of either S or Na₂SO₄ to the urea-supplemented starter did not improve animal performance, even when 40% of the total protein in the diets was supplied by nonprotein N sources. The urea-supplemented starter rations had N:S ratios before S supplementation of 11.4:1 (experiment (1)) and 9.4:1 (experiment (2)), close to the ratios considered optimum for ruminants.

IT 583-91-5
RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)
(feeding expts. with, on **early**-weaned calf)

RN 583-91-5 HCAPLUS
CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)



L33 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1965:448290 HCAPLUS

DOCUMENT NUMBER: 63:48290

ORIGINAL REFERENCE NO.: 63:8800f-g

TITLE: The development of an amino acid reference diet for the **early** growth of chicks

AUTHOR(S): Dean, W. F.; Scott, H. M.

CORPORATE SOURCE: Univ. of Illinois, Urbana

SOURCE: Poultry Sci. (1965), 44(3), 803-8

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An amino acid diet patterned after the one reported by Greene, et al. (ibid. 39(2), 512-14(1960)) containing the equivalent of 26.20% protein was modified to give maximal growth with minimal levels of amino acids. The final mixture contained the equivalent of 17.6% protein. Expressed as percent of the diet the composition is as follows: L-arginine, 1.10; L-histidine, 0.30; L-lysine, 1.12; L-tyrosine, 0.63; L-tryptophan, 0.225; L-phenylalanine, 0.68; DL-methionine, 0.45; L-cystine, 0.35; L-threonine, 0.65; L-leucine, 1.20; L-isoleucine, 0.80; L-valine, 0.82; glycine, 1.60; L-glutamic acid, 12.00. All assays were conducted in the presence of 1% proline.

IT 583-91-5, Butyric acid, 2-hydroxy-4-(methylthio)-
(feeding expts. with, on chicks)

RN 583-91-5 HCAPLUS

CN Butanoic acid, 2-hydroxy-4-(methylthio)- (9CI) (CA INDEX NAME)

